

SEARCH REQUEST FORM

Scientific and Technical Information Center

Requester's Full Name: Jeffrey E. Russell Examiner #: 6283 Date: 8-14-2002
 Art Unit: 1653 Phone Number 301-5975 Serial Number: 09/786,702
 Mail Box and Bldg/Room Location: _____ Results Format Preferred (circle): PAPER DISK E-MAIL
CI 11 7861 / CI 11 7807

If more than one search is submitted, please prioritize searches in order of need.

Please provide a detailed statement of the search topic, and describe as specifically as possible the subject matter to be searched. Include the elected species or structures, keywords, synonyms, acronyms, and registry numbers, and combine with the concept or utility of the invention. Define any terms that may have a special meaning. Give examples or relevant citations, authors, etc, if known. Please attach a copy of the cover sheet, pertinent claims, and abstract.

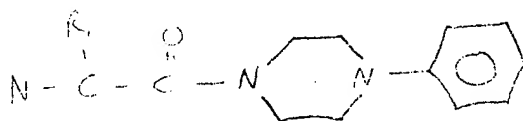
Title of Invention: Pyrazine-4-yl derivatives as inhibitors of the interaction between mdm2 and p53

Inventors (please provide full names): R. Luke, P. Jansburg, R. Cotton

Earliest Priority Filing Date: 3-7-2001

For Sequence Searches Only Please include all pertinent information (parent, child, divisional, or issued patent numbers) along with the appropriate serial number.

Please search the following partial structure:



← ring can be substituted

Keywords are cancer, MDM2, p53. Alternatively, please require R₁ to be -(CH₂)₀₋₃ - ring where the ring is heterocyclic or not, aromatic or not.

Thank you.

JER

STAFF USE ONLY

Searcher: Jeffrey E. Russell

Searcher Phone #: 301-5975

Searcher Location: _____

Date Searcher Picked Up: _____

Date Completed: 8/15/02

Searcher Prep & Review Time: _____

Clerical Prep Time: _____

Online Time: _____

Type of Search

NA Sequence (#) _____

AA Sequence (#) _____

Structure (#) _____

Bibliographic _____

Litigation _____

Fulltext _____

Patent Family _____

Other _____

Vendors and cost where applicable

STN _____

Dialog _____

Questel/Orbit _____

Dr. Link _____

Lexis/Nexis _____

Sequence Systems _____

WWW/Internet _____

Other (specify) _____

=> fil hcaplus
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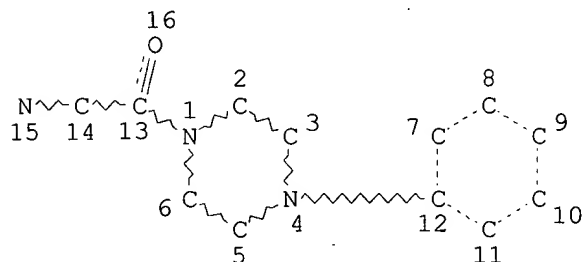
FILE COVERS 1907 - 15 Aug 2002 VOL 137 ISS 7
 FILE LAST UPDATED: 14 Aug 2002 (20020814/ED)

This file contains CAS Registry Numbers for easy and accurate substance identification.

CAS roles have been modified effective December 16, 2001. Please check your SDI profiles to see if they need to be revised. For information on CAS roles, enter HELP ROLES at an arrow prompt or use the CAS Roles thesaurus (/RL field) in this file.

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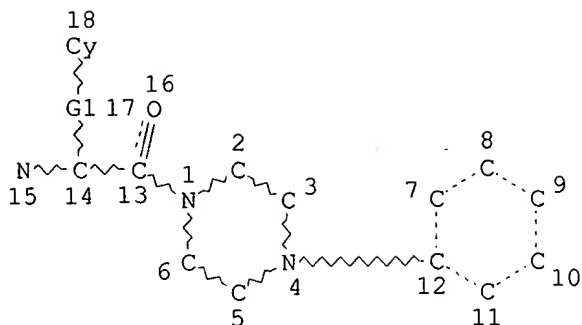
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STEREO ATTRIBUTES: NONE
 L4 1670 SEA FILE=REGISTRY SSS FUL L3
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REP G1=(0-2) C
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STEREO ATTRIBUTES: NONE

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 L8 647 SEA FILE=REGISTRY ABB=ON PLU=ON P53/BI
 L9 143 SEA FILE=HCAPLUS ABB=ON PLU=ON L6
 L10 1361 SEA FILE=HCAPLUS ABB=ON PLU=ON L7 OR MDM2
 L11 21884 SEA FILE=HCAPLUS ABB=ON PLU=ON L8 OR P53 OR P(W)53
 L12 2 SEA FILE=HCAPLUS ABB=ON PLU=ON L9 AND (L10 OR L11)

=> d ibib abs hitrn l12 1-2

L12 ANSWER 1 OF 2 HCAPLUS COPYRIGHT 2002 ACS
 ACCESSION NUMBER: 2000:191103 HCAPLUS
 DOCUMENT NUMBER: 132:237374
 TITLE: Preparation of amino acid and peptidyl
 piperazine-4-phenyl derivatives as inhibitors of the
 interaction between MDM2 and p53
 INVENTOR(S): Luke, Richard William Arthur; Jewsbury, Philip John;
 Cotton, Ronald
 PATENT ASSIGNEE(S): Zeneca Ltd., UK
 SOURCE: PCT Int. Appl., 57 pp.
 CODEN: PIXXD2
 DOCUMENT TYPE: Patent
 LANGUAGE: English
 FAMILY ACC. NUM. COUNT: 1
 PATENT INFORMATION:

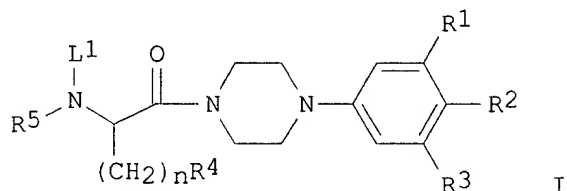
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RW: GH, GM, KE, LS, MW, SD, SL, SZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG,				

CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG
 AU 9957512 A1 20000403 AU 1999-57512 19990907
 EP 1112284 A1 20010704 EP 1999-944688 19990907
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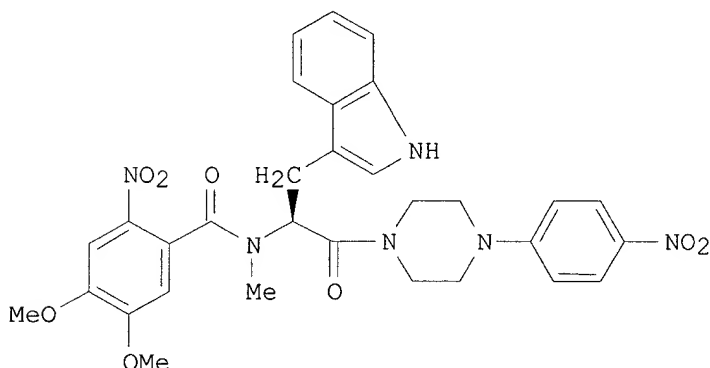
PRIORITY APPLN. INFO.: GB 1998-19860 A 19980912
 WO 1999-GB2957 W 19990907

OTHER SOURCE(S): MARPAT 132:237374

GI



II



AB Title compds. I [L1 = H, Me; R1, R2, R3 = independently H, halo, NO2, CN, (un)substituted C(O)NH2; R4 = indolyl, N-(C1-4alkyl)indolyl, C5-7 carbocyclic ring, or aryl, any of which can be substituted on ring carbon atoms with up to three substituents each independently selected from halo, C1-4alkyl, or C1-4alkoxy; R5 = H, C1-4alkyl, R6CH2, R6C(O), or a peptidyl moiety; R6 = (un)substituted aryl, heteroaryl, or heterocyclyl, aminoC3-6alkyl, N-(C1-4alkyl)aminoC3-6alkyl, or N,N-(diC1-4alkyl)aminoC3-6alkyl; n = 0-2] or their pharmaceutically acceptable salts, prodrugs, or solvates were prepd. as inhibitors of the interaction between **MDM2** and **p53** and may be useful in the treatment of cancers. Thus, II was prepd. by coupling 1-(4-nitrophenyl)piperazine to 4,5-dimethoxy-2-nitrobenzoyl-NMeTrp-OH in DMF using diisopropylethylamine and HATU. The starting material, 4,5-dimethoxy-2-nitrobenzoyl-NMeTrp-OH, was synthesized on an ABI 430 automated peptide synthesizer starting from 2-chlorotritylchloride resin. The inhibition of the **p53/MDM2** interaction was measured using a modified ELISA assay using a histidine tagged **MDM2**, a **p53** GST fusion protein, and a nickel chelate alk. phosphatase. Compds. of formula I possess an IC50 in the range from 0.03 to 200 .mu.M.

IT 261914-53-8P 261914-54-9P 261914-55-0P
 261914-56-1P 261914-57-2P 261914-58-3P
 261914-59-4P 261914-60-7P 261914-61-8P
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261914-65-2P 261914-66-3P 261914-67-4P

261914-68-5P 261914-69-6P 261914-70-9P

RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)

(prepn. of amino acid and peptidyl piperazine-4-Ph derivs. as inhibitors of the interaction between **MDM2** and **p53**)

IT 261914-75-4P 261914-76-5P

RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)

(prepn. of amino acid and peptidyl piperazine-4-Ph derivs. as inhibitors of the interaction between **MDM2** and **p53**)

REFERENCE COUNT: 2 THERE ARE 2 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L12 ANSWER 2 OF 2 HCAPLUS COPYRIGHT 2002 ACS

ACCESSION NUMBER: 1999:790013 HCAPLUS

DOCUMENT NUMBER: 132:233660

TITLE: Effects of the protein kinase inhibitors wortmannin and KN62 on cellular radiosensitivity and radiation-activated S phase and G1/S checkpoints in normal human fibroblasts

AUTHOR(S): Enns, L.; Murray, D.; Mirzayans, R.

CORPORATE SOURCE: Department of Oncology, University of Alberta, Edmonton, AB, T6G 1Z2, Can.

SOURCE: British Journal of Cancer (1999), 81(6), 959-965
CODEN: BJCAAI; ISSN: 0007-0920

PUBLISHER: Churchill Livingstone

DOCUMENT TYPE: Journal

LANGUAGE: English

AB Wortmannin is a potent inhibitor of phosphatidylinositol (PI) 3-kinase and PI 3-kinase-related proteins (e.g. ATM), but it does not inhibit the activity of purified calmodulin-dependent protein kinase II (CaMKII). In the present study, we compared the effects of wortmannin and the CaMKII inhibitor KN62 on the response of normal human dermal fibroblast cultures to .gamma. radiation. We demonstrate that wortmannin confers a phenotype on normal fibroblasts remarkably similar to that characteristic of cells homozygous for the ATM mutation. Thus wortmannin-treated normal fibroblasts exhibit increased sensitivity to radiation-induced cell killing, lack of temporary block in transition from G1 to S phase following irradiation (i.e. impaired G1/S checkpoint), and radioresistant DNA synthesis (i.e. impaired S phase checkpoint). Wortmannin-treated cultures display a diminished capacity for radiation-induced up-regulation of **p53** protein and expression of p21WAF1, a **p53**-regulated gene involved in cell cycle arrest at the G1/S border; the treated cultures also exhibit decreased capacity for enhancement of CaMKII activity post-irradiation, known to be necessary for triggering the S phase checkpoint. We further demonstrate that KN62 confers a radioresistant DNA synthesis phenotype on normal fibroblasts and moderately potentiates their sensitivity to killing by .gamma. rays, without modulating G1/S checkpoint, **p53** up-regulation and p21WAF1 expression following radiation exposure. We conclude that CaMKII is involved in the radiation responsive signalling pathway mediating S phase checkpoint but not in the **p53**-dependent pathway controlling G1/S checkpoint, and that a wortmannin-sensitive kinase functions upstream in both pathways.

IT 127191-97-3, KN62

RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); BIOL (Biological study)

(effects of protein kinase inhibitors on cellular radiosensitivity and radiation-activated S phase and G1/S checkpoints in normal human fibroblasts)

REFERENCE COUNT: 34 THERE ARE 34 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

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=> select hit rn l12 1-2
E1 THROUGH E21 ASSIGNED

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STRUCTURE FILE UPDATES: 14 AUG 2002 HIGHEST RN 443957-06-0
DICTIONARY FILE UPDATES: 14 AUG 2002 HIGHEST RN 443957-06-0

TSCA INFORMATION NOW CURRENT THROUGH MAY 20, 2002

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conducting SmartSELECT searches.

Crossover limits have been increased. See HELP CROSSOVER for details.

Calculated physical property data is now available. See HELP PROPERTIES
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<http://www.cas.org/ONLINE/STN/STNOTES/stnotes27.pdf>

=> d his l13-l14

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L14 21 S L13 AND L6

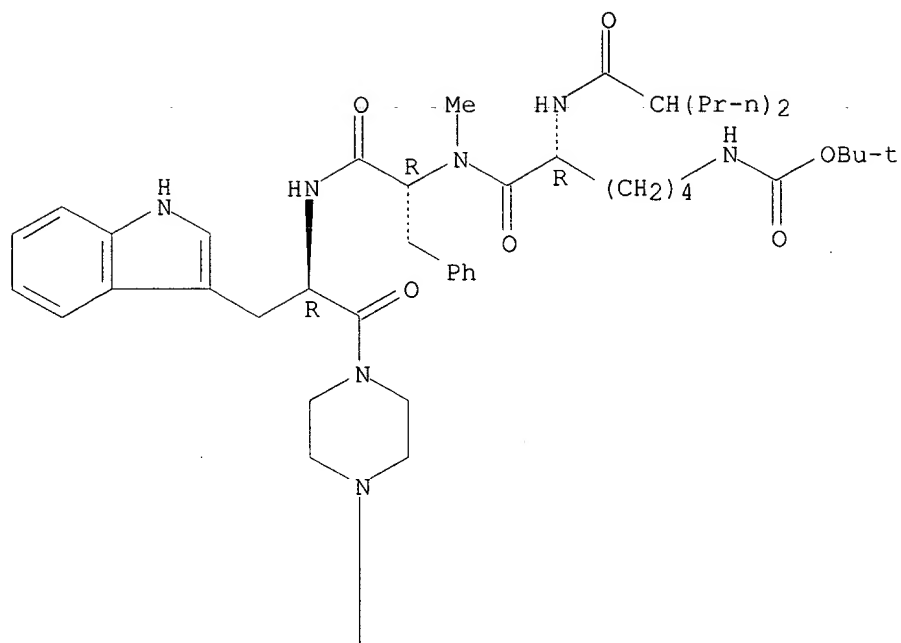
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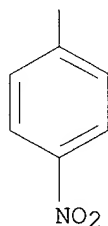
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FS STEREOSEARCH
MF C50 H68 N8 O8
SR CA
LC STN Files: CA, CAPLUS, TOXCENTER

Absolute stereochemistry.

PAGE 1-A



PAGE 2-A



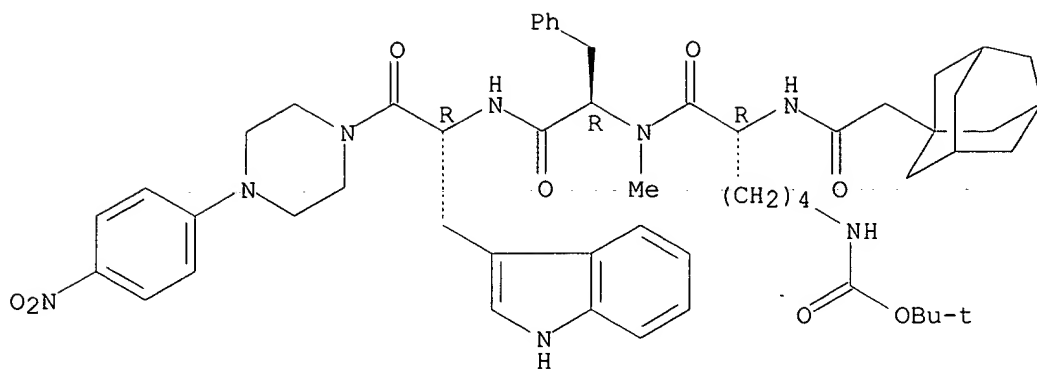
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REFERENCE 1: 132:237374

L14 ANSWER 2 OF 21 REGISTRY COPYRIGHT 2002 ACS
RN **261914-75-4** REGISTRY
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LC STN Files: CA, CAPLUS, TOXCENTER

Absolute stereochemistry.



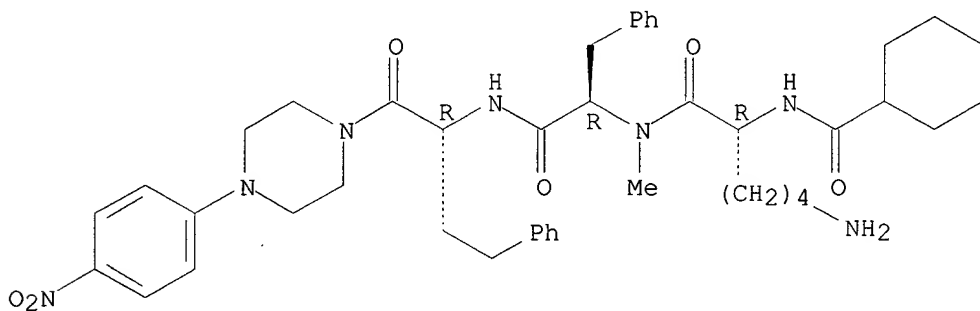
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REFERENCE 1: 132:237374

L14 ANSWER 3 OF 21 REGISTRY COPYRIGHT 2002 ACS
RN **261914-70-9** REGISTRY
CN D-Phenylalaninamide, N2-(cyclohexylcarbonyl)-D-lysyl-N.alpha.-methyl-N-
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LC STN Files: CA, CAPLUS, TOXCENTER

Absolute stereochemistry.



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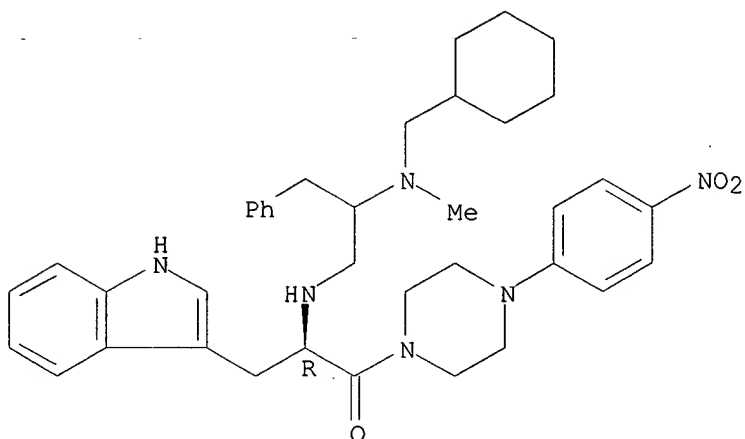
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REFERENCE 1: 132:237374

L14 ANSWER 4 OF 21 REGISTRY COPYRIGHT 2002 ACS
RN **261914-69-6** REGISTRY
CN Piperazine, 1-[(2R)-2-[[2-[(cyclohexylmethyl)methylamino]-3-phenylpropyl]amino]-3-(1H-indol-3-yl)-1-oxopropyl]-4-(4-nitrophenyl)- (9CI)
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LC STN Files: CA, CAPLUS, TOXCENTER

Absolute stereochemistry.



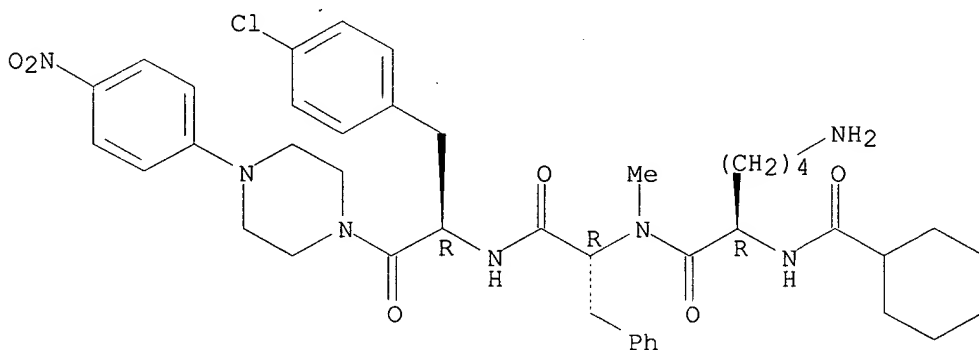
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REFERENCE 1: 132:237374

L14 ANSWER 5 OF 21 REGISTRY COPYRIGHT 2002 ACS
RN **261914-68-5** REGISTRY
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SR CA
LC STN Files: CA, CAPLUS, TOXCENTER

Absolute stereochemistry.



PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

1 REFERENCES IN FILE CA (1967 TO DATE)
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REFERENCE 1: 132:237374

L14 ANSWER 6 OF 21 REGISTRY COPYRIGHT 2002 ACS

RN **261914-67-4** REGISTRY

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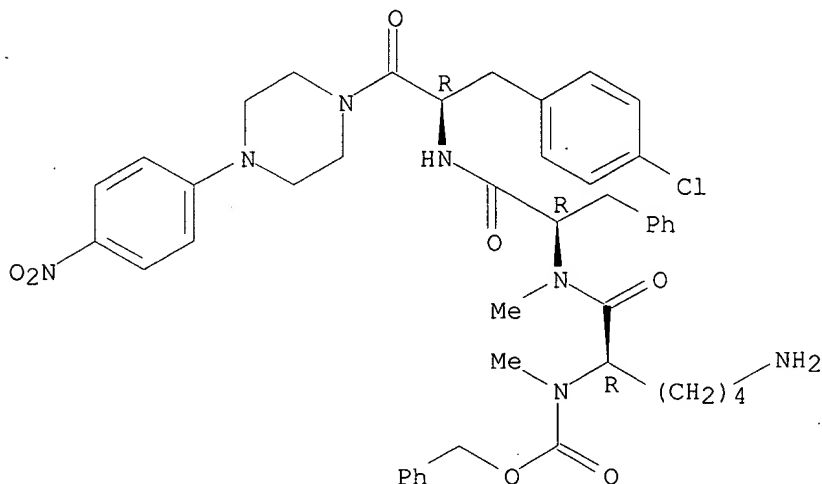
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MF C44 H52 Cl N7 O7

SR CA

LC STN Files: CA, CAPLUS, TOXCENTER

Absolute stereochemistry.



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1 REFERENCES IN FILE CAPLUS (1967 TO DATE)

REFERENCE 1: 132:237374

L14 ANSWER 7 OF 21 REGISTRY COPYRIGHT 2002 ACS

RN **261914-66-3** REGISTRY

CN Carbamic acid, [(1R)-3-amino-1-[[[(1R)-2-[[[(1R)-1-(1H-indol-3-ylmethyl)-2-[4-(4-nitrophenyl)-1-piperazinyl]-2-oxoethyl]amino]-2-oxo-1-(phenylmethyl)ethyl]methylamino]carbonyl]propyl]methyl-, phenylmethyl ester (9CI) (CA INDEX NAME)

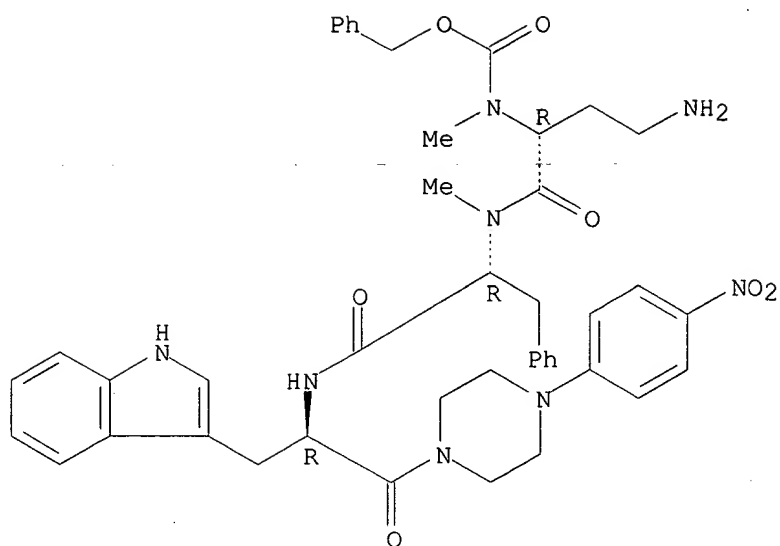
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Absolute stereochemistry.



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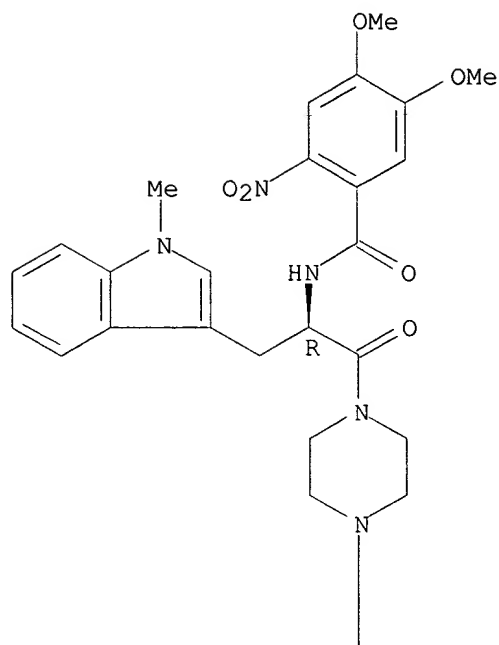
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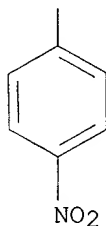
L14 ANSWER 8 OF 21 REGISTRY COPYRIGHT 2002 ACS
RN **261914-65-2** REGISTRY
CN Benzamide, 4,5-dimethoxy-N-[(1R)-1-[(1-methyl-1H-indol-3-yl)methyl]-2-[4-(4-nitrophenyl)-1-piperazinyl]-2-oxoethyl]-2-nitro- (9CI) (CA INDEX NAME)
FS STEREOSEARCH
MF C31 H32 N6 O8
SR CA
LC STN Files: CA, CAPLUS, TOXCENTER

Absolute stereochemistry.

PAGE 1-A



PAGE 2-A



PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

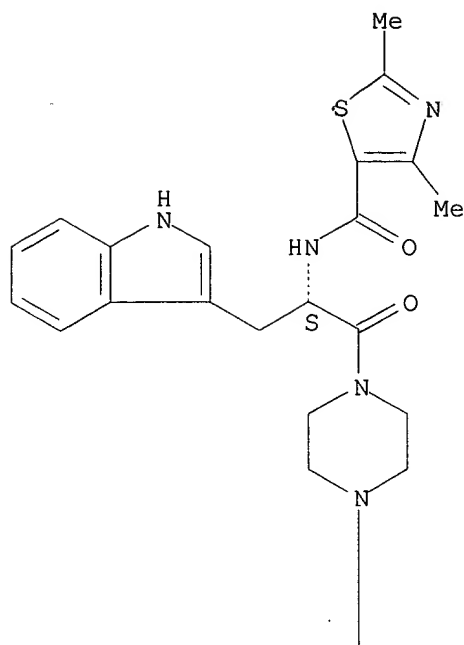
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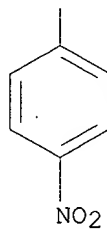
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FS STEREOSEARCH
MF C27 H28 N6 O4 S
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LC STN Files: CA, CAPLUS, TOXCENTER

Absolute stereochemistry.

PAGE 1-A



PAGE 2-A



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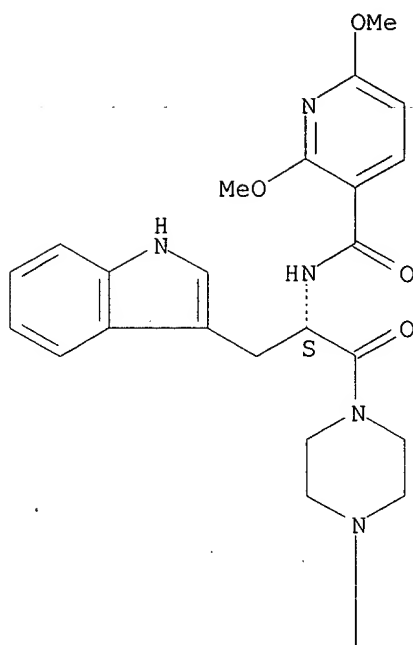
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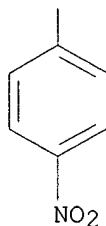
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Absolute stereochemistry.

PAGE 1-A



PAGE 2-A



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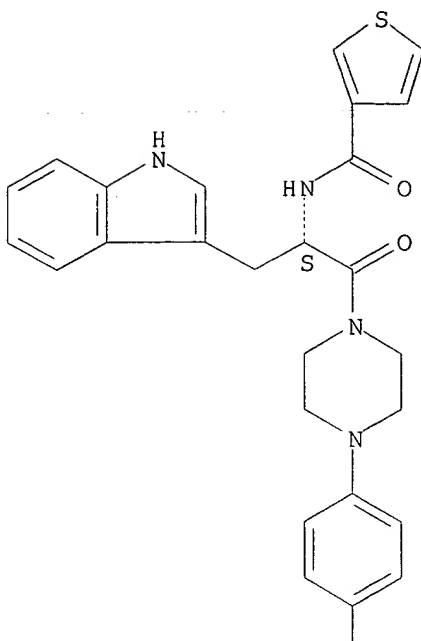
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Absolute stereochemistry.

PAGE 1-A



PAGE 2-A

NO₂

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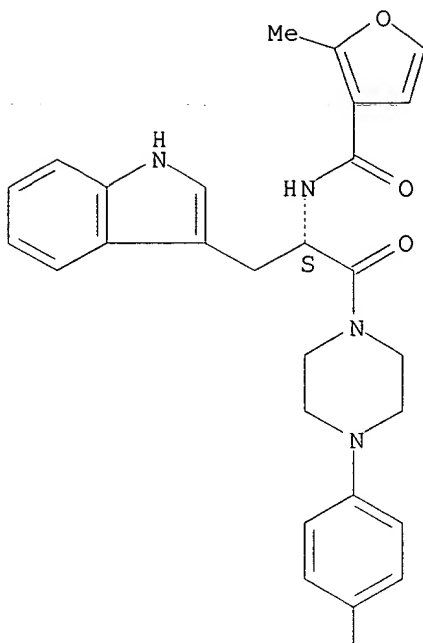
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REFERENCE 1: 132:237374

L14 ANSWER 12 OF 21 REGISTRY COPYRIGHT 2002 ACS
RN **261914-61-8** REGISTRY
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FS STEREOSEARCH
MF C27 H27 N5 O5
SR CA
LC STN Files: CA, CAPLUS, TOXCENTER

Absolute stereochemistry.

PAGE 1-A



PAGE 2-A

NO₂

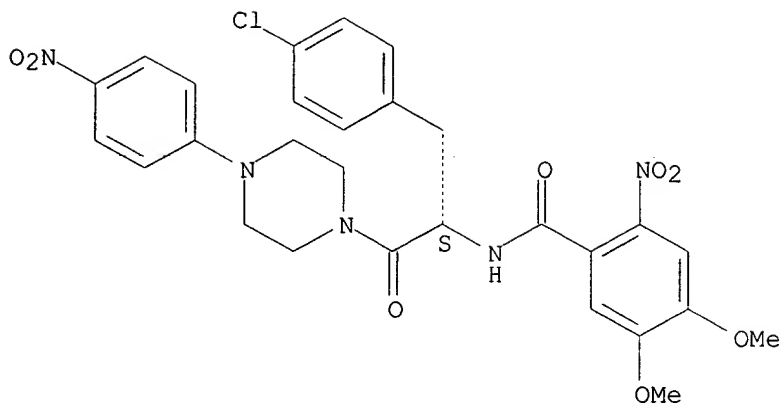
PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

1 REFERENCES IN FILE CA (1967 TO DATE)
1 REFERENCES IN FILE CAPLUS (1967 TO DATE)

REFERENCE 1: 132:237374

L14 ANSWER 13 OF 21 REGISTRY COPYRIGHT 2002 ACS
RN **261914-60-7** REGISTRY
CN Benzamide, N-[(1S)-1-[(4-chlorophenyl)methyl]-2-[4-(4-nitrophenyl)-1-piperazinyl]-2-oxoethyl]-4,5-dimethoxy-2-nitro- (9CI) (CA INDEX NAME)
FS STEREOSEARCH
MF C28 H28 Cl N5 O8
SR CA
LC STN Files: CA, CAPLUS, TOXCENTER

Absolute stereochemistry.



PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

1 REFERENCES IN FILE CA (1967 TO DATE)
1 REFERENCES IN FILE CAPLUS (1967 TO DATE)

REFERENCE 1: 132:237374

L14 ANSWER 14 OF 21 REGISTRY COPYRIGHT 2002 ACS

RN **261914-59-4** REGISTRY

CN Benzamide, N-[(1S)-1-(1H-indol-3-ylmethyl)-2-[4-(4-nitrophenyl)-1-piperazinyl]-2-oxoethyl]-4,5-dimethoxy-N-methyl-2-nitro- (9CI) (CA INDEX NAME)

FS STEREOSEARCH

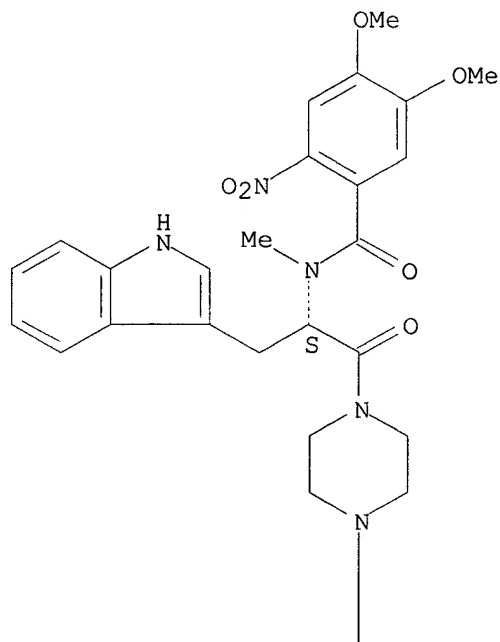
MF C31 H32 N6 O8

SR CA

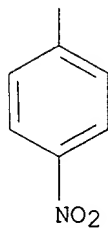
LC STN Files: CA, CAPLUS, TOXCENTER

Absolute stereochemistry.

PAGE 1-A



PAGE 2-A



PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

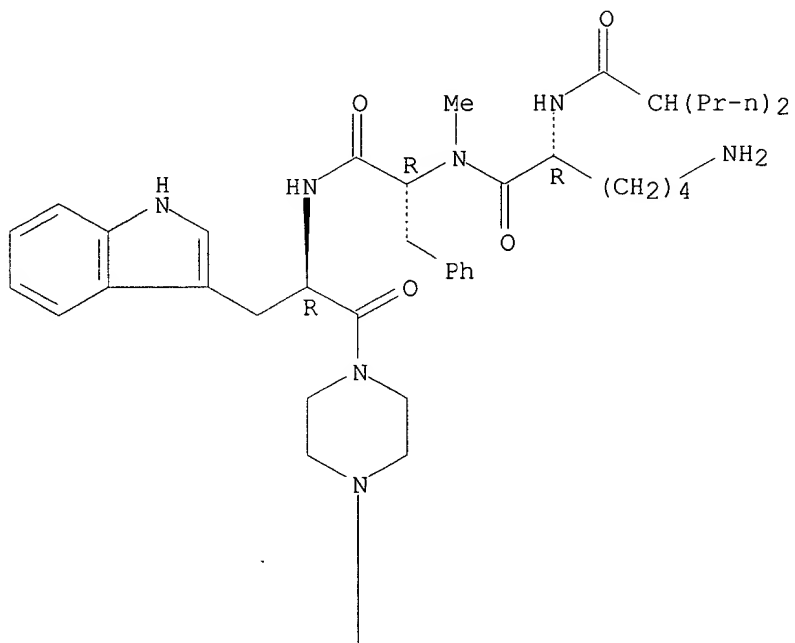
1 REFERENCES IN FILE CA (1967 TO DATE)
1 REFERENCES IN FILE CAPLUS (1967 TO DATE)

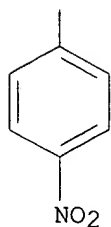
REFERENCE 1: 132:237374

L14 ANSWER 15 OF 21 REGISTRY COPYRIGHT 2002 ACS
RN **261914-58-3** REGISTRY
CN D-Phenylalaninamide, N2-(1-oxo-2-propylpentyl)-D-lysyl-N-[(1R)-1-(1H-indol-3-ylmethyl)-2-[4-(4-nitrophenyl)-1-piperazinyl]-2-oxoethyl]-N.alpha.-methyl- (9CI) (CA INDEX NAME)
FS STEREOSEARCH
MF C45 H60 N8 O6
SR CA
LC STN Files: CA, CAPLUS, TOXCENTER

Absolute stereochemistry.

PAGE 1-A





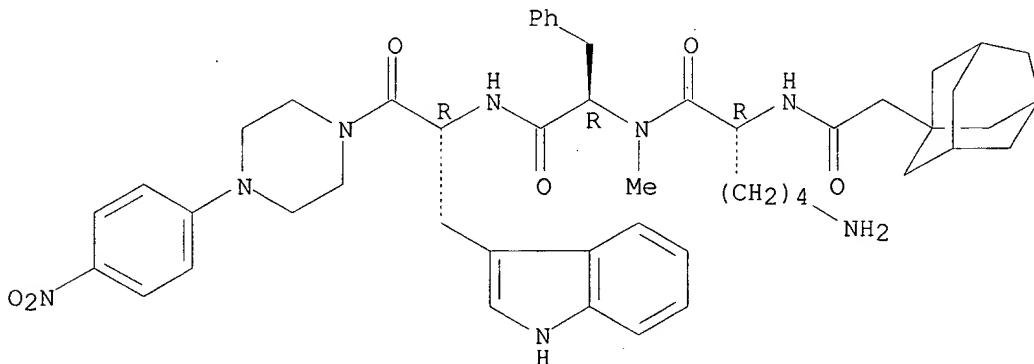
PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

1 REFERENCES IN FILE CA (1967 TO DATE)
1 REFERENCES IN FILE CAPLUS (1967 TO DATE)

REFERENCE 1: 132:237374

L14 ANSWER 16 OF 21 REGISTRY COPYRIGHT 2002 ACS
RN **261914-57-2** REGISTRY
CN D-Phenylalaninamide, N2-(tricyclo[3.3.1.1^{3,7}]dec-1-ylacetyl)-D-lysyl-N-[(1R)-1-(1H-indol-3-ylmethyl)-2-[4-(4-nitrophenyl)-1-piperazinyl]-2-oxoethyl]-N.alpha.-methyl- (9CI) (CA INDEX NAME)
FS STEREOSEARCH
MF C49 H62 N8 O6
SR CA
LC STN Files: CA, CAPLUS, TOXCENTER

Absolute stereochemistry.



PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

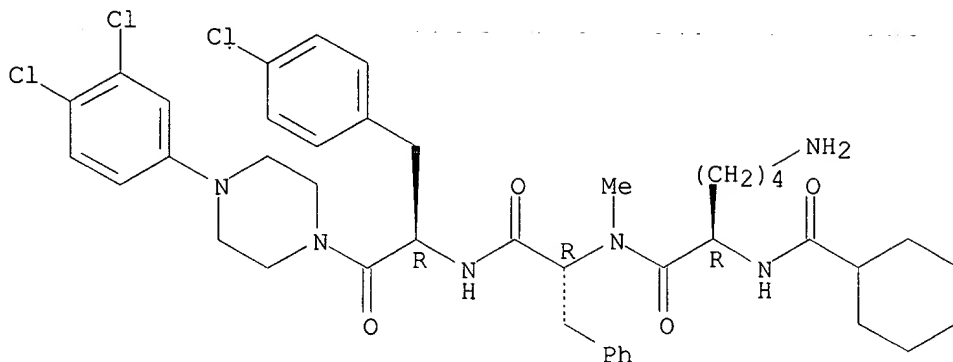
1 REFERENCES IN FILE CA (1967 TO DATE)
1 REFERENCES IN FILE CAPLUS (1967 TO DATE)

REFERENCE 1: 132:237374

L14 ANSWER 17 OF 21 REGISTRY COPYRIGHT 2002 ACS
RN **261914-56-1** REGISTRY
CN D-Phenylalaninamide, N2-(cyclohexylcarbonyl)-D-lysyl-N-[(1R)-1-[(4-chlorophenyl)methyl]-2-[4-(3,4-dichlorophenyl)-1-piperazinyl]-2-oxoethyl]-N.alpha.-methyl- (9CI) (CA INDEX NAME)
FS STEREOSEARCH
MF C42 H53 Cl3 N6 O4

SR CA
LC STN Files: CA, CAPLUS, TOXCENTER

Absolute stereochemistry.



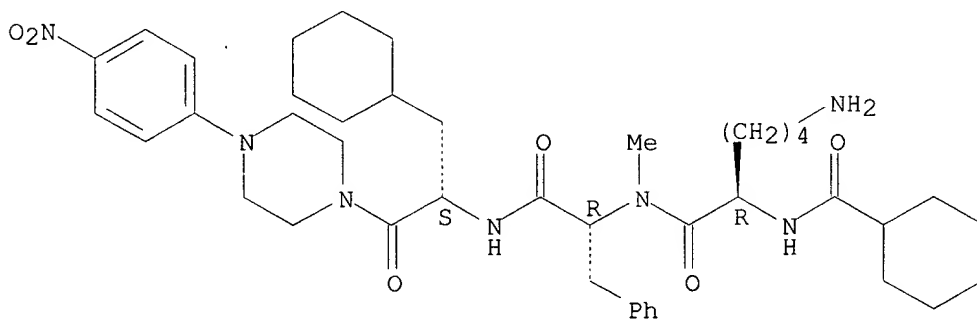
PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

1 REFERENCES IN FILE CA (1967 TO DATE)
1 REFERENCES IN FILE CAPLUS (1967 TO DATE)

REFERENCE 1: 132:237374

L14 ANSWER 18 OF 21 REGISTRY COPYRIGHT 2002 ACS
RN 261914-55-0 REGISTRY
CN D-Phenylalaninamide, N2-(cyclohexylcarbonyl)-D-lysyl-N-[(1S)-1-(cyclohexylmethyl)-2-[4-(4-nitrophenyl)-1-piperazinyl]-2-oxoethyl]-N.alpha.-methyl- (9CI) (CA INDEX NAME)
FS STEREOSEARCH
MF C42 H61 N7 O6
SR CA
LC STN Files: CA, CAPLUS, TOXCENTER

Absolute stereochemistry.



PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

1 REFERENCES IN FILE CA (1967 TO DATE)
1 REFERENCES IN FILE CAPLUS (1967 TO DATE)

REFERENCE 1: 132:237374

L14 ANSWER 19 OF 21 REGISTRY COPYRIGHT 2002 ACS
RN 261914-54-9 REGISTRY

O=[N+]([O-])c1ccc(cc1)N2CCN(CC2)C(=O)S[C@H](N)CC3CCCCC3

1 REFERENCES IN FILE CA (1967 TO DATE)
1 REFERENCES IN FILE CAPLUS (1967 TO DATE)

```
L14  ANSWER 20 OF 21  REGISTRY  COPYRIGHT 2002 ACS
RN   261914-53-8  REGISTRY
CN   Carbamic acid, [(1R)-3-amino-1-[[[(1R)-2-[(1R)-1-[(4-chlorophenyl)methyl]-
2-[4-(4-nitrophenyl)-1-piperazinyl]-2-oxoethyl]amino]-2-oxo-1-
(phenylmethyl)ethyl]methylamino]carbonyl]propyl]methyl-, phenylmethyl
ester (9CI)  (CA INDEX NAME)
FS   STEREOSEARCH
MF   C42 H48 Cl N7 O7
SR   CA
LC   STN Files:  CA, CAPLUS, TOXCENTER
```

The chemical structure is a complex molecule with multiple stereocenters. It features a p-nitrophenyl group connected to a piperidine ring. The piperidine ring is linked via a carbonyl group to a chiral center (R) which is also bonded to a hydrogen atom (HN) and a 4-chlorophenyl group. This chiral center is further connected to another chiral center (R) which is bonded to a phenyl group (Ph) and a nitrogen atom. The nitrogen atom is part of a side chain containing two methyl groups (Me), a carbonyl group (C=O), and a 3-aminopropyl group (CH₂CH₂CH₂NH₂). The side chain also includes a benzyl ester group (PhCH₂OC(=O)-). The stereochemistry is indicated by wedges and dashes at several chiral centers.

PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

1 REFERENCES IN FILE CA (1967 TO DATE)
1 REFERENCES IN FILE CAPLUS (1967 TO DATE)

REFERENCE 1: 132:237374

L14 ANSWER 21 OF 21 REGISTRY COPYRIGHT 2002 ACS

RN 127191-97-3 REGISTRY

CN 5-Isoquinolinesulfonic acid, 4-[(2S)-2-[(5-isoquinolinylsulfonyl)methylamino]-3-oxo-3-(4-phenyl-1-piperazinyl)propyl]phenyl ester (9CI) (CA INDEX NAME)

OTHER CA INDEX NAMES:

CN 5-Isoquinolinesulfonic acid, 4-[2-[(5-isoquinolinylsulfonyl)methylamino]-3-oxo-3-(4-phenyl-1-piperazinyl)propyl]phenyl ester, (S)-

OTHER NAMES:

CN KN 62

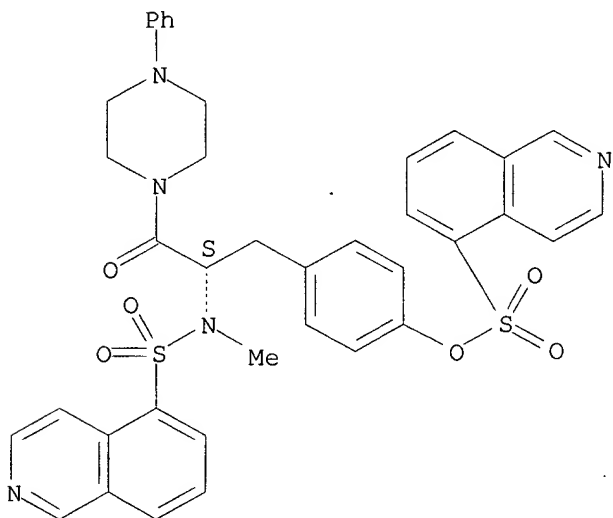
FS STEREOSEARCH

MF C38 H35 N5 O6 S2

SR CA

LC STN Files: BIOSIS, BIOTECHNO, CA, CANCERLIT, CAPLUS, CHEMCATS, CSCHEM, DDFU, DRUGU, EMBASE, MEDLINE, TOXCENTER, USPATFULL

Absolute stereochemistry.



PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

74 REFERENCES IN FILE CA (1967 TO DATE)
75 REFERENCES IN FILE CAPLUS (1967 TO DATE)

REFERENCE 1: 136:310127

REFERENCE 2: 136:177996

REFERENCE 3: 136:177560

REFERENCE 4: 136:112684

REFERENCE 5: 135:223282

REFERENCE 6: 135:133334

REFERENCE 7: 134:216948

REFERENCE 8: 134:202393

REFERENCE 9: 134:188207

REFERENCE 10: 134:67957

=> fil hcaplus
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 FILE LAST UPDATED: 14 Aug 2002 (20020814/ED)

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 =>

=> d stat que l16 nos
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 L4 1670 SEA FILE=REGISTRY SSS FUL L3
 L5 STR
 L6 471 SEA FILE=REGISTRY SUB=L4 SSS FUL L5
 L7 57 SEA FILE=REGISTRY ABB=ON PLU=ON MDM2/BI
 L8 647 SEA FILE=REGISTRY ABB=ON PLU=ON P53/BI
 L9 143 SEA FILE=HCAPLUS ABB=ON PLU=ON L6
 L10 1361 SEA FILE=HCAPLUS ABB=ON PLU=ON L7 OR MDM2
 L11 21884 SEA FILE=HCAPLUS ABB=ON PLU=ON L8 OR P53 OR P(W)53
 L12 2 SEA FILE=HCAPLUS ABB=ON PLU=ON L9 AND (L10 OR L11)
 L15 6 SEA FILE=HCAPLUS ABB=ON PLU=ON L9(L) (?CANCER? OR ?TUMOR? OR ?MALIG? OR ?NEOPLAS?)
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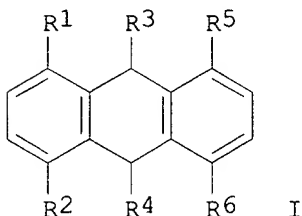
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L16 ANSWER 1 OF 6 HCAPLUS COPYRIGHT 2002 ACS
 ACCESSION NUMBER: 2001:453018 HCAPLUS
 DOCUMENT NUMBER: 135:46452
 TITLE: Preparation of aminoanthracenediones and amino acid and peptide conjugates thereof as anticancer and antimicrobial agents.
 INVENTOR(S): Mincher, David John; Turnbull, Agnes; Kay, Graeme Gillies
 PATENT ASSIGNEE(S): BTG International Limited, UK
 SOURCE: PCT Int. Appl., 77 pp.
 CODEN: PIXXD2
 DOCUMENT TYPE: Patent
 LANGUAGE: English

FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2001044190	A1	20010621	WO 2000-GB4829	20001215
<p>W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CR, CU, CZ, DE, DK, DM, DZ, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM</p> <p>RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG</p>				
PRIORITY APPLN. INFO.:			GB 1999-29801	A 19991216
OTHER SOURCE(S):		MARPAT 135:46452		
GI				



AB Use of title compds. [I; .gtoreq.1 of R1, R2, R5, R6 = AB, the others = H, OH, alkoxy, acyloxy, AB = Z(R7)nXY; R7 = divalent org. radical; n = 0, 1; R3, R4 = H, OH, O; A = Z(R7)nX; X = O, NH, CO; B = amino acid residue, peptide group, or isostere thereof; Y = H; capping group; Z = amino group incorporating a (substituted) heterocyclic or carbocyclic ring] or a physiol. acceptable deriv. of such compd. for the manuf. of a medicament for the treatment of cancers or microbial infections having cells exhibiting topoisomerase I is claimed. Thus, trans-1,4-diaminocyclohexane reacted with 1-chloroanthraquinone to give 1-[(4-aminocyclohexyl)amino]anthracene. The latter was coupled with N-tert-butoxycarbonyl L-4-chlorophenylalanine N-hydroxysuccinimide followed by deprotection to give (2S)-2-amino-N-[4-[(9,10-dioxoanthryl)amino]cyclohexyl]-3-(4-chlorophenyl)propionamide trifluoroacetate. This inhibited MAC15 colon adenocarcinoma with IC50 = 1.0 .mu.M.

IT 345265-71-6P 345265-73-8P

RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(prepn. of aminoanthracenediones and amino acid and peptide conjugates thereof as **anticancer** and antimicrobial agents)

REFERENCE COUNT: 5 THERE ARE 5 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L16 ANSWER 2 OF 6 HCAPLUS COPYRIGHT 2002 ACS

ACCESSION NUMBER: 2000:10569 HCAPLUS

DOCUMENT NUMBER: 132:77621

TITLE: Method for inducing monocytes to exhibit the phenotype of activated myeloid dendritic cells

INVENTOR(S): Cohen, Peter A.; Czerniecki, Brian J.; Koski, Gary K.; Weng, David E.; Carter, Charles; Ojeifo, John O.; Schwartz, Gretchen N.

PATENT ASSIGNEE(S): United States Dept. of Health and Human Services, USA
 SOURCE: U.S., 37 pp., Cont.-in-part of U.S. 5,643,786.
 CODEN: USXXAM
 DOCUMENT TYPE: Patent
 LANGUAGE: English
 FAMILY ACC. NUM. COUNT: 3
 PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 6010905	A	20000104	US 1997-885671	19970630
US 5643786	A	19970701	US 1995-379227	19950127
WO 9900137	A2	19990107	WO 1998-US13542	19980630
WO 9900137	A3	20000106		
W: AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GE, GH, GM, GW, HU, ID, IL, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, US, UZ, VN, YU, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, GM, KE, LS, MW, SD, SZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG				
AU 9882746	A1	19990119	AU 1998-82746	19980630
EP 998298	A2	20000510	EP 1998-932972	19980630
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, FI				
JP 2002511870	T2	20020416	JP 1999-505868	19980630
US 6358736	B1	20020319	US 1999-401060	19990922
PRIORITY APPLN. INFO.:				
			US 1995-379227	A2 19950127
			US 1997-885617	A3 19970630
			US 1997-885671	A2 19970630
			WO 1998-US13542	W 19980630
AB The present invention relates to methods of increasing the antigen presenting ability of monocytes by contacting them with an agent which increases the intracellular calcium level. Methods of obtaining the monocytes are also disclosed. In addn., the present invention relates to methods of inducing bone marrow progenitor cells and endothelial cells to express mols. involved in generating immune responses. Methods of modulating the expression of mols. involved in generating immune responses are also disclosed, as are methods of treating cancer and leukemia.				
IT 127191-97-3, KN 62				
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses) (calcium ionophore for increasing antigen presenting ability of monocytes to treat leukemia and cancer)				
REFERENCE COUNT: 27 THERE ARE 27 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT				
L16 ANSWER 3 OF 6 HCAPLUS COPYRIGHT 2002 ACS				
ACCESSION NUMBER: 1998:507740 HCAPLUS				
DOCUMENT NUMBER: 129:225386				
TITLE: Tumor cell resistance to topoisomerase II poisons: role for intracellular free calcium in the sensitization by inhibitors of calcium-calmodulin-dependent enzymes				
AUTHOR(S): Grabowski, Dale R.; Dubyak, George R.; Rybicki, Lisa; Hidaka, Hiroyoshi; Ganapathi, Ram				
CORPORATE SOURCE: Cleveland Clinic Foundation, Experimental Therapeutics Program, Cancer Center, Cleveland, OH, 44195, USA				
SOURCE: Biochemical Pharmacology (1998), 56(3), 345-349 CODEN: BCPCA6; ISSN: 0006-2952				
PUBLISHER: Elsevier Science Inc.				
DOCUMENT TYPE: Journal				
LANGUAGE: English				

AB Tumor cell resistance to inhibitors of topoisomerase II (topo II) is assocd. frequently with the overexpression of P-glycoprotein (PGP), and strategies to overcome resistance are focused on restoring defects in drug accumulation. Inhibitors of calcium-calmodulin-dependent enzymes sensitize resistant tumor cells to the topo II poison etoposide (VP-16) by enhancing DNA damage and an apoptotic response. In the present study, the authors have investigated the consequences of buffering intracellular calcium with 1,2-bis(o-aminophenoxy)ethane-N,N,N',N'-tetraacetic acid tetra(acetoxy-methyl) ester (BAPTA-AM) on the sensitizing effects of the calmodulin-dependent protein kinase II inhibitor 1-[N,O-bis(1,5-isoquinolinesulfonyl)-N-methyl-L-tyrosyl]-4-piperazine (KN-62) in etoposide-resistant human leukemia HL-60 (HL-60/ADR0.05) cells. In cells pretreated with 20 .mu.M BAPTA-AM for 2 h, extracellular ATP failed to trigger intracellular calcium transients, and no effects on the accumulation of VP-16 were apparent. Also, the effect of KN-62 in significantly (to 0.042) enhancing the accumulation of VP-16 in HL-60/ADR0.05 cells was unaffected due to pretreatment with BAPTA-AM. In contrast, pretreatment with BAPTA-AM reduced the DNA damage induced by VP-16, and significantly reversed the enhancement by KN-62 of VP-16-stabilized topo II-mediated DNA cleavable complex formation. The pretreatment of HL-60/ADR0.05 cells with BAPTA-AM was also assocd. with the hypophosphorylation of topo II.alpha.. Consistent with the ability of BAPTA-AM to circumvent the potentiation by KN-62 of VP-16-induced DNA damage, survival of cells treated with 40 .mu.M VP-16 in the absence of KN-62 and 10 .mu.M VP-16 in the presence of KN-62 was significantly (to 0.031) higher due to BAPTA-AM pretreatment. Results demonstrate that intracellular calcium transients could play a key role in the sensitization of etoposide-resistant tumor cells by inhibitors of calcium-calmodulin-dependent enzymes.

IT 127191-97-3

RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)

(tumor cell resistance to topoisomerase II poisons and role for intracellular free calcium in sensitization by inhibitors of calcium-calmodulin-dependent enzymes in relation to DNA damage)

L16 ANSWER 4 OF 6 HCAPLUS COPYRIGHT 2002 ACS

ACCESSION NUMBER: 1998:437165 HCAPLUS

DOCUMENT NUMBER: 129:157089

TITLE: Calcium/calmodulin kinase inhibitors and immunosuppressant macrolides rapamycin and FK506 inhibit progestin- and glucocorticosteroid receptor-mediated transcription in human breast cancer T47D cells

AUTHOR(S): Le Bihan, Stephane; Marsaud, Veronique; Mercier-Bodard, Christine; Baulieu, Etienne-Emile; Mader, Sylvie; White, John H.; Renoir, Jack-Michel

CORPORATE SOURCE: URA 1218 Centre Nationale de la Recherche Scientifique, Pharmacologie Cellulaire, Chatenay-Malabry, 92296, Fr.

SOURCE: Molecular Endocrinology (1998), 12(7), 986-1001
CODEN: MOENEN; ISSN: 0888-8809

PUBLISHER: Endocrine Society

DOCUMENT TYPE: Journal

LANGUAGE: English

AB The effects of immunosuppressants and inhibitors of specific calcium/calmodulin kinase (CaMK) of types II and IV on progestin/glucocorticosteroid-induced transcription were studied in two human stably transfected breast cancer T47D cell lines. The lines contain the chloramphenicol acetyltransferase (CAT) gene under control either of the mouse mammary tumor virus promoter (T47D- MMTV-CAT), or the minimal promoter contg. five glucocorticosteroid/progestin hormone response

elements [T47D-(GRE)5-CAT]. Progesterin- and triamcinolone acetonide (TA)-induced CAT gene expression was inhibited in a dose-dependent manner in both lines by preincubation with rapamycin (Rap) and, to a lesser extent, with FK506, but not with cyclosporin A. CaMK II and/or IV inhibitors KN62 and KN93 also inhibited progesterin- and TA-stimulated transcription in both lines. None of these drugs had any effect on basal transcription. The antagonist RU486 inhibited all the effects of both progesterin and TA, suggesting that progesterone receptor (PR)-, as well as glucocorticosteroid receptor (GR)-mediated transactivation are targets of immunosuppressants and CaMKs in T47D cells. Indeed, Northern anal. showed that Rap, KN62, and, to a lesser degree, FK506 inhibited progesterin stimulation of Cyclin D1 mRNA levels, but not those of the non-steroid-regulated glyceraldehyde 3-phosphate dehydrogenase (GAPDH) gene. Addn. of Rap or KN62 after exposure of cells to progesterone agonist Org 2058 had no effect on induction of CAT activity. Taken together, these data indicate that Rap and FK506, as well as CaMK inhibitors, inhibit steroid-induced activities of exogenous, as well as of some endogenous, steroid receptor-regulated genes by a mechanism preceding hormone-induced receptor activation. Rap appeared to stabilize a 9S form of [3H]Org 2058-PR complexes isolated from T47D (GRE)5CAT cell nuclei. By contrast, the progesterone receptor (PR) was isolated from cells treated with KN62 as a 5S entity, undistinguishable from the 5S PR species extd. from cells treated with progesterin only. The nuclear 9S-[3H]Org2058-PR resulting from cells exposed to Rap, contained, in addn. to the heat shock proteins of 90 kDa and 70 kDa (hsp90 and hsp70), the FK506-binding immunophilin FKBP52 but not FKBP51, although the latter was part of unliganded PR heterocomplex assocd. with hsp90. These results suggest that Rap and KN62 act upon the PR by distinct mechanisms, with only Rap impeding progesterin-induced PR transformation. FKBP51 appeared to dissociate from the receptor heterocomplex, but not from hsp90, after hormone binding to PR in vitro and in vivo, whether in the presence or not of Rap and KN62. Immunopptn. expts. distinguished two PR- and glucocorticosteroid (GR)-assocd. mol. chaperone complexes, contg. hsp90 and hsp70 and FKBP52 or FKBP51. Another complex identified in T47D cytosol contained hsp90 and the cyclosporin A-binding cyclophilin of 40 kDa, CYP40, but not hsp70, PR, or GR. These observations support the concept that FKBP51 and FKBP52 can act as regulators of Rap and FK506 activity upon PR and GR-mediated transcription, a mechanism that could be also regulated by type II and/or type IV CaMKs.

IT 127191-97-3, KN62

RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); BIOL (Biological study)
(calcium/calmodulin kinase inhibitors and immunosuppressant macrolides inhibit progesterin- and glucocorticosteroid receptor-mediated transcription in human breast **cancer** T47D cells and role of immunophilins and heat shock proteins)

L16 ANSWER 5 OF 6 HCAPLUS COPYRIGHT 2002 ACS

ACCESSION NUMBER: 1995:866429 HCAPLUS

DOCUMENT NUMBER: 123:306132

TITLE: Effect of KN-62, Ca²⁺/calmodulin-dependent protein kinase II inhibitor, on adriamycin resistance of human ovarian cancer cells

AUTHOR(S): Obata, Naoko Hasegawa; Okazaki, Katsuo; Maeda, Osamu; Kikkawa, Fumitaka; Tomoda, Yutaka; Hidaka, Hiroyoshi

CORPORATE SOURCE: Department Obstetrics Gynecology, Nagoya University School Medicine, Nagoya, 466, Japan

SOURCE: Biochem. Biophys. Res. Commun. (1995), 215(2), 566-71
CODEN: BBRCA9; ISSN: 0006-291X

DOCUMENT TYPE: Journal

LANGUAGE: English

AB We examd. effects of an isoquinolinesulfonamide deriv., KN-62, on human ovarian cancer cells, NOS3AR, that are resistant to Adriamycin (ADR). MTT

assay revealed that 10 .mu.M KN-62 overcame the resistance. KN-62 had little effect on GST activity. In studies on the intracellular accumulation of ADR, KN-62 increased the ADR contents in the resistant cells close to the level seen in the sensitive cells. These results suggest that the reversal of the resistance against ADR in ovarian cancer cells by KN-62 is mainly due to higher accumulation of ADR in NOS3AR cells. Furthermore, we detected Ca2+/calmodulin-dependent protein kinase II (CaM kinase II) in NOS3AR cells since KN-62 is a specific inhibitor of the kinase. This paper discusses modulation of ADR-resistance by KN-62.

IT 127191-97-3, KN-62

RL: BAC (Biological activity or effector, except adverse); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(effect of KN-62, a Ca2+/calmodulin-dependent protein kinase II inhibitor, on adriamycin resistance of human ovarian **cancer** cells)

L16 ANSWER 6 OF 6 HCAPLUS COPYRIGHT 2002 ACS

ACCESSION NUMBER: 1981:175538 HCAPLUS
DOCUMENT NUMBER: 94:175538
TITLE: Tumor-resolving and histolytic medicaments comprising dehydrooligopeptides
INVENTOR(S): Etschenberg, Eugen; Opitz, Wolfgang; Raddatz, Siegfried
PATENT ASSIGNEE(S): Troponwerke G.m.b.H. und Co. K.-G., Fed. Rep. Ger.
SOURCE: Brit., 48 pp.
CODEN: BRXXAA
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 3
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
GB 1570140	A	19800625	GB 1977-53179	19771221
DE 2659154	A1	19780706	DE 1976-2659154	19761228
DE 2745673	A1	19790412	DE 1977-2745673	19771011
PRIORITY APPLN. INFO.:			DE 1976-2659154	19761228
			DE 1977-2745673	19771011

AB Pharmaceutical compns. contg. 1-90% wt. of dehydrooligopeptides or their salts, prepd. by alk. hydrolysis of the corresponding 2,4-disubstituted 5(4H)oxazolones or by aminolysis of the oxazolones with the alkali metal salts, esters, or amides of amino acids, showed tumor resolving and histolytic activity with low toxicity and good general tolerance when administered at 1-100 mg/kg/day.

IT 75667-58-2P

RL: SPN (Synthetic preparation); PREP (Preparation)
(prepn. of, for **neoplasm** inhibiting oligopeptides)

=> select hit rn l16 1-6
E22 THROUGH E25 ASSIGNED

=> fil reg
FILE 'REGISTRY' ENTERED AT 19:03:48 ON 15 AUG 2002
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STRUCTURE FILE UPDATES: 14 AUG 2002 HIGHEST RN 443957-06-0
DICTIONARY FILE UPDATES: 14 AUG 2002 HIGHEST RN 443957-06-0

TSCA INFORMATION NOW CURRENT THROUGH MAY 20, 2002

Please note that search-term pricing does apply when conducting SmartSELECT searches.

Crossover limits have been increased. See HELP CROSSOVER for details.

Calculated physical property data is now available. See HELP PROPERTIES for more information. See STNote 27, Searching Properties in the CAS Registry File, for complete details:
<http://www.cas.org/ONLINE/STN/STNOTES/stnotes27.pdf>

=> s e22-e25

1 127191-97-3/BI
 (127191-97-3/RN)
 1 345265-71-6/BI
 (345265-71-6/RN)
 1 345265-73-8/BI
 (345265-73-8/RN)
 1 75667-58-2/BI
 (75667-58-2/RN)

L17 4 (127191-97-3/BI OR 345265-71-6/BI OR 345265-73-8/BI OR 75667-58-2/BI)

=> d ide can l17 1-4

L17 ANSWER 1 OF 4 REGISTRY COPYRIGHT 2002 ACS

RN 345265-73-8 REGISTRY

CN Piperazine, 1-[(2S)-2-amino-1-oxo-3-phenylpropyl]-4-(9,10-dihydro-9,10-dioxo-1-anthracenyl)-, mono(trifluoroacetate) (9CI) (CA INDEX NAME)

FS STEREOSEARCH

MF C27 H25 N3 O3 . C2 H F3 O2

SR CA

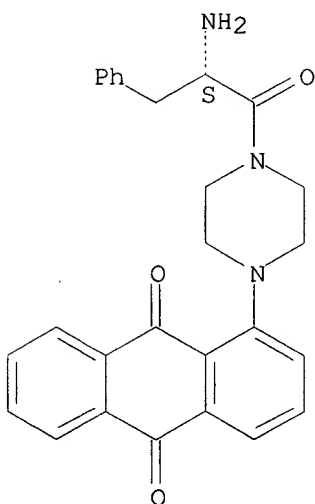
LC STN Files: CA, CAPLUS, TOXCENTER

CM 1

CRN 345265-72-7

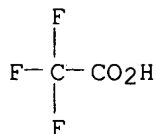
CMF C27 H25 N3 O3

Absolute stereochemistry.



CM 2

CRN 76-05-1
CMF C2 H F3 O2

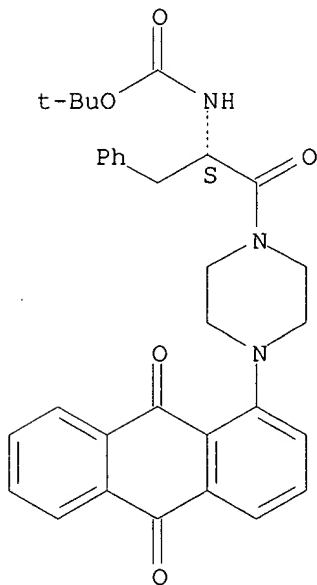


1 REFERENCES IN FILE CA (1967 TO DATE)
1 REFERENCES IN FILE CAPLUS (1967 TO DATE)

REFERENCE 1: 135:46452

L17 ANSWER 2 OF 4 REGISTRY COPYRIGHT 2002 ACS
RN 345265-71-6 REGISTRY
CN Carbamic acid, [(1S)-2-[4-(9,10-dihydro-9,10-dioxo-1-anthracenyl)-1-piperazinyl]-2-oxo-1-(phenylmethyl)ethyl]-, 1,1-dimethylethyl ester (9CI)
(CA INDEX NAME)
FS STEREOSEARCH
MF C32 H33 N3 O5
SR CA
LC STN Files: CA, CAPLUS, TOXCENTER

Absolute stereochemistry.



PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

1 REFERENCES IN FILE CA (1967 TO DATE)
1 REFERENCES IN FILE CAPLUS (1967 TO DATE)

REFERENCE 1: 135:46452

L17 ANSWER 3 OF 4 REGISTRY COPYRIGHT 2002 ACS
RN 127191-97-3 REGISTRY

CN 5-Isoquinolinesulfonic acid, 4-[(2S)-2-[(5-isoquinolinylsulfonyl)methylamino]-3-oxo-3-(4-phenyl-1-piperazinyl)propyl]phenyl ester (9CI) (CA INDEX NAME)

OTHER CA INDEX NAMES:

CN 5-Isoquinolinesulfonic acid, 4-[2-[(5-isoquinolinylsulfonyl)methylamino]-3-oxo-3-(4-phenyl-1-piperazinyl)propyl]phenyl ester, (S)-

OTHER NAMES:

CN KN 62

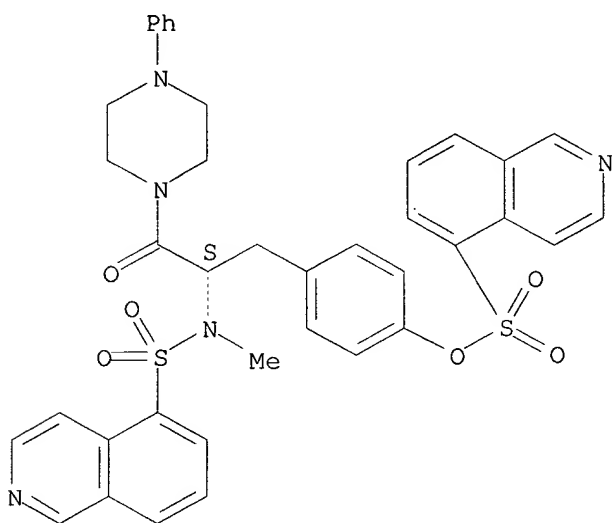
FS STEREOSEARCH

MF C38 H35 N5 O6 S2

SR CA

LC STN Files: BIOSIS, BIOTECHNO, CA, CANCERLIT, CAPLUS, CHEMCATS, CSCHEM, DDFU, DRUGU, EMBASE, MEDLINE, TOXCENTER, USPATFULL

Absolute stereochemistry.



PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

74 REFERENCES IN FILE CA (1967 TO DATE)

75 REFERENCES IN FILE CAPLUS (1967 TO DATE)

REFERENCE 1: 136:310127
 REFERENCE 2: 136:177996
 REFERENCE 3: 136:177560
 REFERENCE 4: 136:112684
 REFERENCE 5: 135:223282
 REFERENCE 6: 135:133334
 REFERENCE 7: 134:216948
 REFERENCE 8: 134:202393
 REFERENCE 9: 134:188207

REFERENCE 10: 134:67957

L17 ANSWER 4 OF 4 REGISTRY COPYRIGHT 2002 ACS

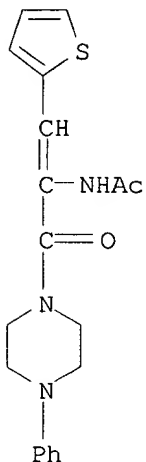
RN 75667-58-2 REGISTRY

CN Acetamide, N-[1-[(4-phenyl-1-piperazinyl)carbonyl]-2-(2-thienyl)ethenyl]-
(9CI) (CA INDEX NAME)

FS 3D CONCORD

MF C19 H21 N3 O2 S

LC STN Files: CA, CAPLUS, TOXCENTER, USPATFULL



PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

2 REFERENCES IN FILE CA (1967 TO DATE)

2 REFERENCES IN FILE CAPLUS (1967 TO DATE)

REFERENCE 1: 97:72781

REFERENCE 2: 94:175538

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L5          STR
L6          471 SEA FILE=REGISTRY SUB=L4 SSS FUL L5
L7          57 SEA FILE=REGISTRY ABB=ON PLU=ON MDM2/BI
L8          647 SEA FILE=REGISTRY ABB=ON PLU=ON P53/BI
L9          143 SEA FILE=HCAPLUS ABB=ON PLU=ON L6
L10         1361 SEA FILE=HCAPLUS ABB=ON PLU=ON L7 OR MDM2
L11         21884 SEA FILE=HCAPLUS ABB=ON PLU=ON L8 OR P53 OR P(W)53
L12         2 SEA FILE=HCAPLUS ABB=ON PLU=ON L9 AND (L10 OR L11)
L15         6 SEA FILE=HCAPLUS ABB=ON PLU=ON L9(L) (?CANCER? OR ?TUMOR? OR
          ?MALIG? OR ?NEOPLAS?)
L16         6 SEA FILE=HCAPLUS ABB=ON PLU=ON L15 NOT L12
L18         1199 SEA FILE=REGISTRY ABB=ON PLU=ON L4 NOT L6
L19         110 SEA FILE=HCAPLUS ABB=ON PLU=ON L18
L21         10 SEA FILE=HCAPLUS ABB=ON PLU=ON (L19 AND (?CANCER? OR ?TUMOR?
          OR ?MALIG? OR ?NEOPLAS? OR L10 OR L11)) NOT (L12 OR L16)
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=> d ibib abs hitrn 121 1-10

L21 ANSWER 1 OF 10 HCAPLUS COPYRIGHT 2002 ACS
 ACCESSION NUMBER: 2002:157727 HCAPLUS
 DOCUMENT NUMBER: 136:216538
 TITLE: Preparation and use of aryl amides as factor Xa
 inhibitors
 INVENTOR(S): Cappi, Michael W.; Fuchs, Thilo; Eckl, Robert;
 Schabbert, Silke
 PATENT ASSIGNEE(S): Morphochem A.-G., Germany
 SOURCE: PCT Int. Appl., 44 pp.
 CODEN: PIXXD2
 DOCUMENT TYPE: Patent
 LANGUAGE: German
 FAMILY ACC. NUM. COUNT: 1
 PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2002016312	A2	20020228	WO 2001-EP9753	20010823
WO 2002016312	A3	20020620		
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
DE 10041402	A1	20020314	DE 2000-10041402	20000823
AU 2001095507	A5	20020304	AU 2001-95507	20010823
PRIORITY APPLN. INFO.:			DE 2000-10041402 A	20000823
			WO 2001-EP9753 W	20010823
OTHER SOURCE(S):			MARPAT 136:216538	
GI				

* STRUCTURE DIAGRAM TOO LARGE FOR DISPLAY - AVAILABLE VIA OFFLINE PRINT *

AB Title compds. I [X = Cl, Br, R1N=C(NH2); R1 = H, OH, carboxy, alkyl, aralkyl, arylalkoxy, heteroalkyl, etc.; Ar = (hetero)arylene, heteroarylalkylene, arylalkylene; X = arom. ring; R3 = H, (hetero)alkyl, aralkyl; R4 = OH, NH2, heteroalkyl, carbocyclic, etc.; n = 0-5; R5 = H, alkyl, heteroalkyl, carbocyclic, heterocycloalkyl, aryl, heteroaryl, heteroarylalkyl, aralkyl; R6-7 = H, alkyl, heteroalkyl, carbocyclic, heterocycloalkyl, etc.; R8 = H, alkyl, heteroalkyl, carbocyclic, heterocycloalkyl, aryl, heteroaryl, heteroarylalkyl, aralkyl or together with R5 forms a heterocycloalkyl ring system] were prepd. E.g., II was prepd. from helicin, 3-aminobenzamidine dihydrochloride and 2-isocyano-1-[4-(2-methoxyphenyl)piperazin-1-yl]ethanone in MeOH after 24 h at room temp. Compds. of the invention had IC50 = 1 nM to 1 .mu.M for factor Xa. I are useful for preventing and/or treating thrombo-embolic illnesses.

IT 401914-24-7P

RL: PAC (Pharmacological activity); RCT (Reactant); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); RACT (Reactant or reagent); USES (Uses)
(drug; prepn. and use of aryl amides as factor Xa inhibitors)

IT 401914-18-9P 401914-19-0P 401914-20-3P,
2-Biphenyl-4-yl-2-(3-carbamimidoylphenylamino)-N-[2-[4-(2-methoxyphenyl)piperazin-1-yl]-2-oxoethyl]acetamide 401914-21-4P
401914-22-5P, 2-(3-Carbamimidoylphenylamino)-2-(3,4-dimethoxyphenyl)-N-[2-[4-(2-methoxyphenyl)piperazin-1-yl]-2-oxoethyl]acetamide 401914-23-6P 401914-25-8P
401914-26-9P 401914-27-0P 401914-28-1P
401914-29-2P 401914-30-5P 401914-32-7P
401914-33-8P 401914-34-9P 401914-35-0P
401914-37-2P, 2-(3-Carbamimidoylphenylamino)-N-[2-[4-(2-nitrophenyl)piperazin-1-yl]-2-oxoethyl]-2-phenylacetamide
401914-38-3P, 2-(3-Carbamimidoylphenylamino)-N-[2-[4-(2,4-difluorophenyl)piperazin-1-yl]-2-oxoethyl]-2-phenylacetamide
401914-39-4P 401914-41-8P 401914-43-0P
401914-44-1P 401914-45-2P 401914-46-3P
401914-47-4P 401914-48-5P 401914-49-6P
401914-50-9P 401914-52-1P 401914-53-2P
401914-54-3P 401914-56-5P 401914-57-6P
401914-58-7P 401914-59-8P 401914-60-1P
401914-61-2P 401914-67-8P 401914-68-9P
401914-69-0P

RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(drug; prepn. and use of aryl amides as factor Xa inhibitors)

IT 401914-17-8, 2-Isocyanato-1-[4-(2-methoxyphenyl)piperazin-1-yl]ethanone

RL: RCT (Reactant); RACT (Reactant or reagent)
(reactant; prepn. and use of aryl amides as factor Xa inhibitors)

L21 ANSWER 2 OF 10 HCAPLUS COPYRIGHT 2002 ACS

ACCESSION NUMBER: 2001:565040 HCAPLUS

DOCUMENT NUMBER: 135:152817

TITLE: Preparation of pyrido[2,3-d]pyrimidine-2,7-diamine kinase inhibitors for treatment of proliferative disorders

INVENTOR(S): Booth, Richard John; Dobrusin, Ellen Myra; Josyula, Vara Prasad Venkata Nagendra; McNamara, Dennis Joseph; Toogood, Peter Laurence

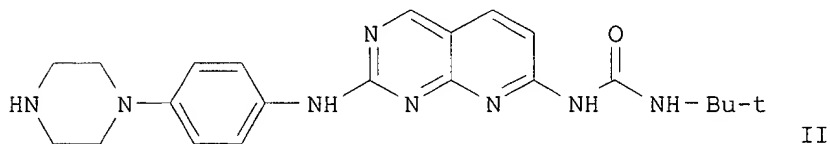
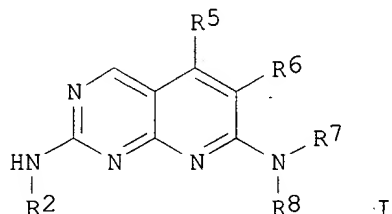
PATENT ASSIGNEE(S): Warner-Lambert Company, USA

SOURCE: PCT Int. Appl., 114 pp.

DOCUMENT TYPE: Patent
 LANGUAGE: English
 FAMILY ACC. NUM. COUNT: 1
 PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2001055147	A1	20010802	WO 2001-IB69	20010123
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CR, CU, CZ, DE, DK, DM, DZ, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
PRIORITY APPLN. INFO.:			US 2000-178261P P 20000125	
OTHER SOURCE(S):			MARPAT 135:152817	

GI



AB Title compds. (I) [wherein R2, R7, R13, R14, and R15 = independently H, or (un)substituted alkyl, alkenyl, alkynyl, or (CH2)_nR12; R5 = halo, CN, NO2, R9, NR9R10, or OR9; R6 = halo, CN, NO2, R9, NR9R10, OR9, CO2R9, COR9, CONR9R10, NR9COR10, or (un)substituted alkenyl or alkynyl; R8 = CO2R13, COR13, CONR13R14, CSNR13R14, C(NR13)NR14R15, SO3R13, SO2R13, SO2NR13R14, PO3R13R14, POR13R14, or PO(NR13R14)₂; R9 and R10 = independently H or (un)substituted alkyl; R11 = heteroaryl or heterocyclic group; R12 = cycloalkyl, heterocyclic, or (hetero)aryl group; n = 0-3; and pharmaceutically acceptable salts, esters, amides, and prodrugs thereof] were prepd. and formulated as cyclin dependent kinase (cdk) and growth factor-mediated tyrosine kinase inhibitors. For example, the 2-methylsulfinyl group of 2-methanesulfinylpyrido[2,3-d]pyrimidin-7-ylamine was displaced by 4-(4-aminophenyl)piperazine-1-carboxylic acid tert-Bu ester (multi-step prepn. of starting materials given) by refluxing in DMSO (36%). The pyrido[2,3-d]pyrimidin-7-amine was converted to the urea by reaction with tert-Bu isocyanate (67.9%) and the piperazine deprotected using HCl/dioxane (93.4%) to afford II.bul.2.1HCl. The latter inhibited the cyclin dependent kinases cdk1/B, cdk2/A, cdk2/E, and cdk4D with IC50 values of 0.219 .mu.M, 0.060 .mu.M, 0.130 .mu.M, and 0.006 .mu.M, resp. In addn., II.bul.2.1HCl inhibited the growth factor receptor tyrosine kinases PDGF-.beta. and FGF-1 by 94.4% and 93.7%, resp., at 50 .mu.M. I are useful for treating cell proliferative disorders, such as

cancer and restenosis (no data).

IT 352328-15-5P
 RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
 (formulation component; prepn. of pyrido[2,3-d]pyrimidine-2,7-diamines kinase inhibitors by cyclization of 3-[2-(methylsulfinyl)-4-aminopyrimidin-5-yl]acrylates or [2,4-diaminopyrimidine-5-yl]ketones)

IT 352328-16-6P
 RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
 (prepn. of pyrido[2,3-d]pyrimidine-2,7-diamines kinase inhibitors by cyclization of 3-[2-(methylsulfinyl)-4-aminopyrimidin-5-yl]acrylates or [2,4-diaminopyrimidine-5-yl]ketones)

REFERENCE COUNT: 8 THERE ARE 8 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L21 ANSWER 3 OF 10 HCAPLUS COPYRIGHT 2002 ACS

ACCESSION NUMBER: 2001:495110 HCAPLUS
 DOCUMENT NUMBER: 135:226981
 TITLE: Design, synthesis, and structure-activity relationships of macrocyclic hydroxamic acids that inhibit **tumor** necrosis factor .alpha. release in vitro and in vivo
 AUTHOR(S): Xue, Chu-Biao; Voss, Matthew E.; Nelson, David J.; Duan, James J.-W.; Cherney, Robert J.; Jacobson, Irina C.; He, Xiaohua; Roderick, John; Chen, Lihua; Corbett, Ronald L.; Wang, Li; Meyer, Dayton T.; Kennedy, Kenneth; DeGrado, William F.; Hardman, Karl D.; Teleha, Christopher A.; Jaffee, Bruce D.; Liu, Rui-Qin; Copeland, Robert A.; Covington, Maryanne B.; Christ, David D.; Trzaskos, James M.; Newton, Robert C.; Magolda, Ronald L.; Wexler, Ruth R.; Decicco, Carl P.
 CORPORATE SOURCE: Experimental Station, DuPont Pharmaceuticals Company, Wilmington, DE, 19880-0500, USA
 SOURCE: Journal of Medicinal Chemistry (2001), 44(16), 2636-2660
 CODEN: JMCMAR; ISSN: 0022-2623
 PUBLISHER: American Chemical Society
 DOCUMENT TYPE: Journal
 LANGUAGE: English

AB To search for TNF-.alpha. (**tumor** necrosis factor .alpha.) converting enzyme (TACE) inhibitors, the authors designed a new class of macrocyclic hydroxamic acids by linking the residues of acyclic anti-succinate-based hydroxamic acids. A variety of residues including amide, carbamate, alkyl, sulfonamido, Boc-amino, and amino were found to be suitable linkers. With an N-methylamide group present, the 13-16-membered macrocycles prepd. exhibited low micromolar activities in the inhibition of TNF-.alpha. release from LPS-stimulated human whole blood. Further elaboration using the cyclophane and cyclic carbamate templates led to the identification of a no. of potent analogs with IC50 values of .ltoreq.0.2 .mu.M in whole blood assay (WBA). A glycine residue was identified as a crit. structural component to achieve both good in vitro potency and good oral activity. The N-methylamide glycine residue attached to the macrocycle provided the best cyclophane analog, SL422 (WBA IC50 = 0.22 .mu.M, LPS-mouse ED50 = 15 mg/kg, po), whereas a morpholinylamide group afforded the most potent and most orally active cyclic carbamate analog, SP057 (WBA IC50 = 0.067 .mu.M, LPS-mouse ED50 = 2.3 mg/kg, po). Further profiling for SL422 and SP057 showed that these macrocyclic compds. are potent TACE inhibitors, with Ki values of 12 and 4.2 nM in the porcine TACE assay, and are broad-spectrum MMP inhibitors.

Pharmacokinetic studies in beagle dogs revealed that SL422 and SP057 are orally bioavailable, with oral bioavailabilities of 11% and 23%, resp.

IT 215938-51-5P

RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); BIOL (Biological study); PREP (Preparation)

(prepn., **tumor** necrosis factor .alpha. converting enzyme inhibitory activity, and structure-activity relationship of macrocyclic hydroxamic acids)

IT 359821-44-6

RL: RCT (Reactant); RACT (Reactant or reagent)

(prepn., **tumor** necrosis factor .alpha. converting enzyme inhibitory activity, and structure-activity relationship of macrocyclic hydroxamic acids)

REFERENCE COUNT: 43 THERE ARE 43 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L21 ANSWER 4 OF 10 HCAPLUS COPYRIGHT 2002 ACS

ACCESSION NUMBER: 2001:416930 HCAPLUS

DOCUMENT NUMBER: 135:33479

TITLE: Preparation of 1-(2-quinolinyl)-1H-benzimidazoles as antiproliferative agents

INVENTOR(S): Barth, Wayne Ernest; Luzzio, Michael Joseph; Lyssikatos, Joseph Peter

PATENT ASSIGNEE(S): Pfizer Products Inc., USA

SOURCE: PCT Int. Appl., 183 pp.

CODEN: PIXXD2

DOCUMENT TYPE: Patent

LANGUAGE: English

FAMILY ACC. NUM. COUNT: 1

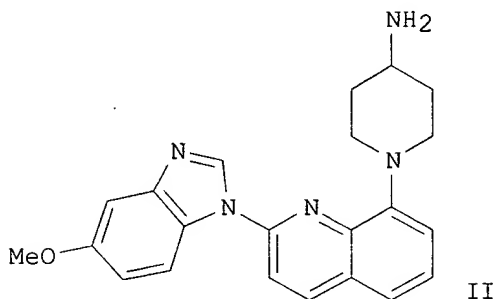
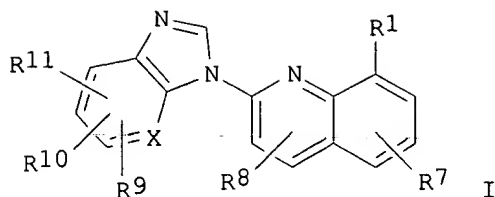
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2001040217	A1	20010607	WO 2000-IB1636	20001110
W:	AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CR, CU, CZ, DE, DK, DM, DZ, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM			
RW:	GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG			

PRIORITY APPLN. INFO.: US 1999-168217P P 19991130

OTHER SOURCE(S): MARPAT 135:33479

GI



AB Title compds. (I) [wherein X = CH or N; R1 = (un)substituted (CR4R5)tCOOR3, (CR4R5)tCONR3R4, (CR4R5)tOR3, or (CR4R5)t(acyl), wherein (CR4R5)t groups may be unsatd.; t = 0-5; R2, R7, R8, R9, R10, and R11 = independently H, (cyclo)alkyl, alkenyl, alkynyl, oxo, halo, CN, NO2, CF3, OCHF2, OCF3, N3, OR3, COR3, COOR3, NR4SO2R6, SO2NR3R4, NR4COR3, CONR3R4, NR5CONR3R4, NR3R4, etc.; R3 = independently H or (un)substituted alkyl, (CR4R5)m(aryl), or (CR4R5)m(heterocyclyl); m = 0-4; R4 and R5 = independently H or alkyl; or R4 and R5 together with the C or N to which they are attached may form a 4-10 membered ring; R6 = substituents provided in the definition of R3 except R6 .noteq. H; and pharmaceutically acceptable salts, prodrugs, and solvates thereof] were prepd. as antiproliferative agents. For example, II was formed in a 7-step sequence involving (1) silylation and triflation of 2,8-quinolinediol, (2) addn. of 4-methoxy-2-nitroaniline, (3) redn. to the diamine using Pd/C, (4) cycloaddn. with formamidine acetate to give 2-(5-methoxybenzimidazol-1-yl)quinolin-8-ol, (5) triflation, (6) addn. of piperidin-4-ylcarbamic acid tert-Bu ester, and (7) deprotection using TFA. I inhibited PDGFR.beta. tyrosine kinase activity with IC50 values ranging from 1 nM to 1000 nM. Thus, I are useful for the treatment of diseases involving abnormal cell growth, such as **cancer** (no data).

IT 343788-25-OP 343788-27-2P 343788-29-4P
343788-96-5P 343789-33-3P

RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(prepn. of 1-(2-quinolinyl)-1H-benzimidazole antiproliferative agents from quinolines and anilines)

REFERENCE COUNT: 4 THERE ARE 4 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L21 ANSWER 5 OF 10 HCAPLUS COPYRIGHT 2002 ACS

ACCESSION NUMBER: 2001:396854 HCAPLUS

DOCUMENT NUMBER: 135:19655

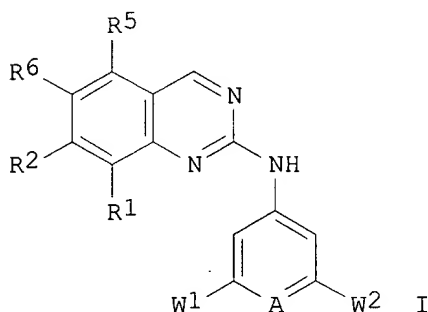
TITLE: Preparation of aminoquinazolines as inhibitors of cyclin-dependent kinases.

INVENTOR(S): Barvian, Mark Robert; Bathini, Yadagiri; Dobrusin, Ellen Myra; Kaltenbronn, James Stanley; Micetich, Ronald George; Sidhu, Inderjit S.; Singh, Rajeshwar; Toogood, Peter Laurence; Winters, Roy Thomas

PATENT ASSIGNEE(S): Warner-Lambert Company, USA

SOURCE: PCT Int. Appl., 102 pp.
 CODEN: PIXXD2
 DOCUMENT TYPE: Patent
 LANGUAGE: English
 FAMILY ACC. NUM. COUNT: 1
 PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2001038315	A1	20010531	WO 2000-US30376	20001103
W: AE, AG, AL, AU, BA, BB, BG, BR, BZ, CA, CN, CR, CU, CZ, DM, DZ, EE, GD, GE, HR, HU, ID, IL, IN, IS, JP, KP, KR, LC, LK, LR, LT, LV, MA, MG, MK, MN, MX, MZ, NO, NZ, PL, RO, SG, SI, SK, SL, TR, TT, UA, US, UZ, VN, YU, ZA, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
BR 2000015718	A	20020723	BR 2000-15718	20001103
PRIORITY APPLN. INFO.:			US 1999-166840P	P 19991122
			WO 2000-US30376	W 20001103
OTHER SOURCE(S):			MARPAT 135:19655	
GI				



AB Title compds. [I; R1 = H, (substituted) alkyl; R2 = OH, alkoxy, aryloxy, NR3R4; A = N, CW3; W1, W2 = H, halo, haloalkyl, NR3R4, NOR3R4, OR3, SR3, COR3, CONR3R4, etc.; R3, R4 = H, alkyl, alkenyl, alkynyl, cycloalkyl, heterocycloalkyl, heteroaryl, etc.; NR3R4 = (substituted) heterocyclcyl; R5 = H, alkyl; R6 = H, alkyl, halo, haloalkyl, alkenyl, alkynyl, COR3, CO2R3, CONR3R4, NR3R4, etc.; W3 = NR3R4, NOR3R4, OH, OR3, SH, SR3, halo, COR3, CO2R3, CONR3R4, etc.], were prepd. Thus, (8-cyclopentyl-7-methoxyquinazolin-2-yl) (4-piperazin-1-ylphenyl)amine (general prepn. given) inhibited CdkB, Cdk2A, Cdk2E, and Cdk4 with IC50 = 0.132 .mu.M, 0.028 .mu.M, 0.250 .mu.M, and 0.001 .mu.M, resp.

IT 342798-47-4P 342798-50-9P 342798-51-0P
 342798-52-1P 342798-53-2P 342798-54-3P
 342798-55-4P 342798-56-5P 342798-89-4P
 342798-90-7P 342798-91-8P 342798-92-9P
 342799-69-3P 342799-70-6P 342799-71-7P
 342799-72-8P 342799-73-9P 342799-74-0P
 342799-75-1P 342799-76-2P 342799-77-3P
 342799-78-4P 342799-79-5P 342799-80-8P
 342799-81-9P 342799-82-0P 342799-83-1P
 342799-84-2P 342799-85-3P 342799-86-4P
 342799-87-5P 342799-88-6P 342799-89-7P
 342799-90-0P 342799-91-1P 342799-92-2P

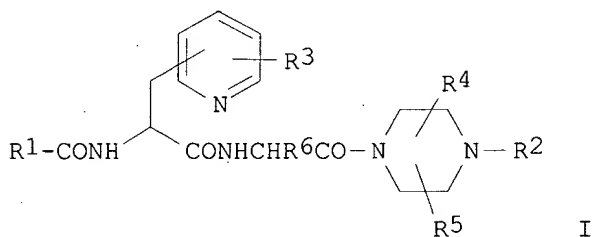
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)

(prepn. of aminoquinazolines as inhibitors of cyclin-dependent kinases)
 REFERENCE COUNT: 5 THERE ARE 5 CITED REFERENCES AVAILABLE FOR THIS
 RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L21 ANSWER 6 OF 10 HCAPLUS COPYRIGHT 2002 ACS

ACCESSION NUMBER: 2001:338558 HCAPLUS
 DOCUMENT NUMBER: 134:340709
 TITLE: Preparation of substituted dipeptides having NOS
 inhibiting activity
 INVENTOR(S): Shima, Ichiro; Ohkawa, Takehiko; Ohne, Kazuhiko; Sato,
 Kentaro; Ishibashi, Naoki; Imamura, Kenichiro
 PATENT ASSIGNEE(S): Fujisawa Pharmaceutical Co., Ltd., Japan
 SOURCE: PCT Int. Appl., 59 pp.
 CODEN: PIXXD2
 DOCUMENT TYPE: Patent
 LANGUAGE: English
 FAMILY ACC. NUM. COUNT: 1
 PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2001032690	A1	20010510	WO 2000-JP7579	20001027
W: BR, CA, CN, JP, KR, US				
RW: AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE				
EP 1226159	A1	20020731	EP 2000-970164	20001027
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, FI, CY				
PRIORITY APPLN. INFO.:			AU 1999-3868	A 19991104
			WO 2000-JP7579	W 20001027
OTHER SOURCE(S):			MARPAT 134:340709	
GI				



AB Dipeptides I [R1 is benzofuranyl or styryl substituted by halogen; R2 is (un)substituted Ph, pyridyl, thienyl, or thiazolyl; R3, R6 = H or lower alkoxy; R4, R5 = H, lower alkyl or optionally protected hydroxy(lower)alkyl] or their pharmaceutically acceptable salts were prepd. for use in the prevention and/or treatment of nitric oxide-mediated diseases. Thus, 5-chloro-N-[(1S)-2-[[2-[4-(4-chlorophenyl)-1-piperazinyl]-2-oxoethyl]amino]-2-oxo-1-(2-pyridylmethyl)ethyl]-1-benzofuran-2-carboxamide (II) was prepd. via amidation reaction and showed 100% inhibition of nitric acid. The combination of compd. II and FK507 dramatically prolonged graft survival in rat cardiac allograft.

IT 337530-26-4P 337530-27-5P 337530-35-5P
 337530-36-6P 337530-38-8P 337530-40-2P
 337530-41-3P 337530-43-5P 337530-44-6P
 337530-63-9P 337530-64-0P 337530-69-5P
 337530-70-8P 337530-75-3P 337530-76-4P
 337530-77-5P 337530-78-6P 337530-79-7P
 337530-80-0P 337530-81-1P 337530-82-2P

RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)

(prepn. of substituted dipeptides having NOS inhibiting activity)

IT 337530-22-0P 337530-23-1P 337530-24-2P
337530-25-3P 337530-65-1P 337530-66-2P
337530-67-3P 337530-68-4P 337530-71-9P
337530-72-0P 337530-73-1P 337530-74-2P

RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)

(prepn. of substituted dipeptides having NOS inhibiting activity)

REFERENCE COUNT: 1 THERE ARE 1 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L21 ANSWER 7 OF 10 HCAPLUS COPYRIGHT 2002 ACS

ACCESSION NUMBER: 2001:152636 HCAPLUS

DOCUMENT NUMBER: 134:208135

TITLE: Preparation of peptidomimetics as inhibitors of tryptase activity

INVENTOR(S): Weber, Lutz; Fuchs, Thilo; Illgen, Katrin; Doemling, Alexander; Cappi, Michael; Nerdinger, Sven

PATENT ASSIGNEE(S): Morphochem A.-G., Germany

SOURCE: PCT Int. Appl., 77 pp.

CODEN: PIXXD2

DOCUMENT TYPE: Patent

LANGUAGE: English

FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2001014320	A1	20010301	WO 2000-EP8238	20000823

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CR, CU, CZ, DE, DK, DM, DZ, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM

RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG

DE 19939910	A1	20010301	DE 1999-19939910	19990823
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EP 1206444	A1	20020522	EP 2000-953198	20000823
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R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL

PRIORITY APPLN. INFO.: DE 1999-19939910 A 19990823
WO 2000-EP8238 W 20000823

OTHER SOURCE(S): MARPAT 134:208135

AB Compds. X-Ar-NR3CHR4CONR8CHR5CONR6R7 [X is H2NC(:NH) or R1N:C(NH2), where R1 is OH, CO2R2, alkyl, aralkyl, aralkyloxy, or heteroalkyl and R2 is alkyl, heteroalkyl, carbocyclyl, heterocycloalkyl, aryl, heteroaryl, or aralkyl; Ar is arylene, heteroarylene, or aralkylene where X is directly attached to the arom. ring system; R3 is H, alkyl, heteroalkyl, or aralkyl; R4 is H, (un)substituted alkyl, heteroalkyl, carbocyclyl, heterocycloalkyl, aryl, heteroaryl, or aralkyl; R5 is H, alkyl, heteroalkyl, carbocyclyl, heterocycloalkyl, aryl, heteroaryl, or aralkyl; R6 and R7 are H, (un)substituted alkyl, heteroalkyl, carbocyclyl, or heterocycloalkyl; R8 is H, alkyl, heteroalkyl, carbocyclyl, heterocycloalkyl, aryl, heteroaryl or aralkyl] or a pharmaceutically acceptable salt, solvate, hydrate or formulation were prepd. as tryptase inhibitors. Thus, a soln. of glycolaldehyde, 3-aminobenzamidine dihydrochloride, and N-[2-(1H-indol-3-yl)ethyl]-3-methylbutanamide-2-isonitrile in methanol, allowed to react for 24 h at room temp. in a

sealed vessel, afforded 2-([2-([3-[amino(imino)methyl]phenyl)amino)-3-hydroxypropanoyl]amino)-N-[2-(1H-indol-3-yl)ethyl]-3-methylbutanamide hydrochloride, which showed IC50 = < 0.09 and 5 .mu.M for inhibition of tryptase and factor Xa, resp.

IT 328550-92-1P 328551-20-8P 328551-48-0P
328552-43-8P

RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)

(prepn. of peptidomimetics as inhibitors of tryptase activity)

REFERENCE COUNT: 3 THERE ARE 3 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L21 ANSWER 8 OF 10 HCAPLUS COPYRIGHT 2002 ACS

ACCESSION NUMBER: 2000:608722 HCAPLUS

DOCUMENT NUMBER: 133:193079

TITLE: Preparation of arylsulfonylheterocyclylhydroxamic acids and related compounds as matrix metalloprotease inhibitors

INVENTOR(S): Barta, Thomas E.; Becker, Daniel P.; Bedell, Louis J.; Boehm, Terri L.; Carroll, Jeffery N.; De Crescenzo, Gary A.; Fobian, Yvette M.; Freskos, John N.; Getman, Daniel P.; McDonald, Joseph J.; Hanson, Gunnar J.; Hockerman, Susan L.; Howard, Susan C.; Kolodziej, Steve A.; Li, Hui; Mischke, Deborah A.; Rico, Joseph G.; Stehle, Nathan W.; Tollefson, Michael B.; Vernier, William F.; Villamil, Clara I.; Rao, Shashidhar N.

PATENT ASSIGNEE(S): G.D. Searle & Co., USA

SOURCE: PCT Int. Appl., 851 pp.

CODEN: PIXXD2

DOCUMENT TYPE: Patent

LANGUAGE: English

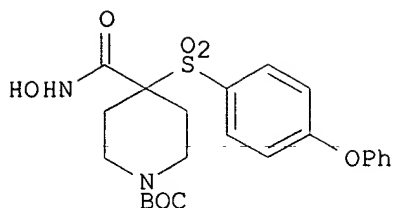
FAMILY ACC. NUM. COUNT: 2

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2000050396	A1	20000831	WO 2000-US2518	20000222
W:	AE, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CR, CU, CZ, DE, DK, DM, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM			
RW:	GH, GM, KE, LS, MW, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG			
US 2001039287	A1	20011108	US 1999-256948	19990224
EP 1230219	A1	20020814	EP 2000-913317	20000222
R:	AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL			
NO 2001003963	A	20011023	NO 2001-3963	20010815
PRIORITY APPLN. INFO.:			US 1999-256948	A 19990224
			US 1997-66007P	P 19971114
			US 1998-95347P	P 19980804
			US 1998-95501P	P 19980806
			US 1998-101080P	P 19980918
			WO 2000-US2518	W 20000222

OTHER SOURCE(S): MARPAT 133:193079

GI



AB A process for treating conditions assocd. with pathol. matrix metalloproteinase (MMP) activity comprises administration of compds. having inhibitory activity against >1 of MMP-2, MMP-9, and MMP-13, while exhibiting substantially less inhibition of MMP-1. The compds. are of the form HONHCOCR1R2SO2R3 [R1, R2 = H; R1R2 = atoms to form a 5-8 membered ring contg. 1-3 heteroatoms; R3 = (substituted) aryl, heteroaryl]. Thus, 4-PhOC6H4SH was heated in Me2SO to give the disulfide dimer, which in THF was added to a mixt. of Et N-tert-butoxycarbonylisonipecotate (prepn. given) and LDA in THF at -60.degree. to room temp. to give 40% sulfide, which was oxidized with m-ClC6H4CO(OOH) to give 59% sulfone. The Et ester was saponified with NaOH in EtOH/H2O to give 100% acid, which in DMF was treated with hydroxybenzotriazole, EDC, 4-methylmorpholine, and aq. NH2OH to give title compd. I. I inhibited MMP-2 with IC50 = 0.2 nM. Pharmacol., pharmacokinetic, and toxicol. data are given for selected compds.

IT 226393-14-2P

RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(prepn. of arylsulfonylheterocyclylhydroxamic acids and related compds. as matrix metalloprotease inhibitors)

REFERENCE COUNT: 7 THERE ARE 7 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L21 ANSWER 9 OF 10 HCAPLUS COPYRIGHT 2002 ACS

ACCESSION NUMBER: 1999:350651 HCAPLUS

DOCUMENT NUMBER: 131:18929

TITLE: Preparation of arylsulfonylheterocyclylhydroxamic acids and related compounds as matrix metalloprotease inhibitors

INVENTOR(S): Barta, Thomas E.; Becker, Daniel P.; Boehm, Terri L.; De Crescenzo, Gary A.; Villamil, Clara I.; McDonald, Joseph J.; Freskos, John N.; Getman, Daniel P.

PATENT ASSIGNEE(S): G.D. Searle & Co., USA

SOURCE: PCT Int. Appl., 840 pp.

CODEN: PIXXD2

DOCUMENT TYPE: Patent

LANGUAGE: English

FAMILY ACC. NUM. COUNT: 2

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9925687	A1	19990527	WO 1998-US23242	19981112
W: AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, US, UZ, VN, YU, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, GM, KE, LS, MW, SD, SZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI,				

CM, GA, GN, GW, ML, MR, NE, SN, TD, TG

CA 2306460	AA	19990527	CA 1998-2306460	19981112
AU 9913732	A1	19990607	AU 1999-13732	19981112
BR 9814643	A	20001003	BR 1998-14643	19981112
EP 1042290	A1	20001011	EP 1998-957485	19981112

R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, PT, IE, FI

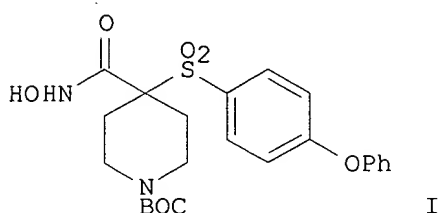
JP 2001523662	T2	20011127	JP 2000-521071	19981112
ZA 9810412	A	19991209	ZA 1998-10412	19981113
US 2001014688	A1	20010816	US 1998-191129	19981113
NO 2000002469	A	20000712	NO 2000-2469	20000512

PRIORITY APPLN. INFO.:

US 1997-66007P	P	19971114
US 1998-95347P	P	19980804
US 1998-95501P	P	19980806
WO 1998-US23242	W	19981112

OTHER SOURCE(S): MARPAT 131:18929

GI



AB A process for treating conditions assocd. with pathol. matrix metalloproteinase (MMP) activity comprises administration of compds. having inhibitory activity against >1 of MMP-2, MMP-9, and MMP-13, while exhibiting substantially less inhibition of MMP-1. The compds. are of the form HONHCOCR1R2SO2R3 [R1, R2 = H; R1R2 = atoms to form a 5-8 membered ring contg. 1-3 heteroatoms; R3 = (substituted) aryl, heteroaryl]. Thus, 4-PhOC6H4SH was heated in Me2SO to give the disulfide dimer, which in THF was added to a mixt. of Et N-tert-butoxycarbonylisonipecotate (prepn. given) and LDA in THF at -60.degree. to room temp. to give 405 sulfide, which was oxidized with m-ClC6H4CO(OOH) to give 59% sulfone. The Et ester was sapond. with NaOH in EtOH/H2O to give 100% acid, which in DMF was treated with hydroxybenzotriazole, EDC, 4-methylmorpholine, and aq. NH2OH to give title compd. (I). I inhibited MMP-2 with IC50 = 0.2 nM.

IT **226393-14-2P**
 RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
 (prepn. of arylsulfonylheterocyclylhydroxamic acids and related compds. as matrix metalloprotease inhibitors)

REFERENCE COUNT: 6 THERE ARE 6 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L21 ANSWER 10 OF 10 HCAPLUS COPYRIGHT 2002 ACS

ACCESSION NUMBER: 1998:761877 HCAPLUS
 DOCUMENT NUMBER: 130:14260
 TITLE: Novel macrocyclic compounds as metalloprotease inhibitors

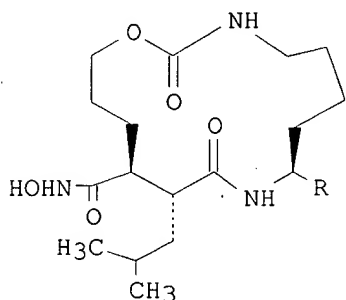
INVENTOR(S): Xue, Chu-Bio; Decicco, Carl P.; Cherney, Robert J.; Arner, Elizabeth; Degrado, William F.; Duan, Jingwu; He, Xiaohua; Jacobson, Irina Cipora; Magolda, Ronald L.; Nelson, David

PATENT ASSIGNEE(S): Dupont Pharmaceuticals Company, USA
 SOURCE: PCT Int. Appl., 80 pp.
 CODEN: PIXXD2

DOCUMENT TYPE: Patent
 LANGUAGE: English
 FAMILY ACC. NUM. COUNT: 3
 PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9851665	A2	19981119	WO 1998-US9789	19980514
WO 9851665	A3	19990325		
W: AU, BR, CA, CN, CZ, EE, HU, IL, JP, KR, LT, LV, MX, NO, NZ, PL, RO, SG, SI, SK, UA, VN, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE				
US 6281352	B1	20010828	US 1997-856223	19970514
AU 9873853	A1	19981208	AU 1998-73853	19980514
EP 981521	A2	20000301	EP 1998-921183	19980514
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, FI				
JP 2001524949	T2	20011204	JP 1998-539935	19980514
PRIORITY APPLN. INFO.:				
			US 1997-856223	A 19970514
			US 1995-6684P	P 19951114
			US 1996-743439	B2 19961101
			WO 1998-US9789	W 19980514

GI



AB Title macrocyclic compds. [I; R = H, CH₃; R₂ = CONHCH₂CH(OH)C₆H₅, CONHCH₂CO₂H, CONHCH₂C₆H₁₁, CONHCH₂-4-CF₃C₆H₄, CO-Asp((CH₃)₃C)-NHCH₃, CONHCH₃, etc.] and their analogs are prep'd. via cyclization, by BOP and diisopropylethylamine, as inhibitors of metalloproteinases involving in tissue degn., including aggrecanase, and the prodn. of **tumor** necrosis factor (TNF). The present invention also relates to pharmaceutical compns. comprising such compds. and to methods of using these compds. for the treatment of inflammatory diseases.

IT 215938-51-5P

RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
 (prepn. of macrocyclic compds. as metalloprotease inhibitors)

=> select hit rn 121 1-10
 E26 THROUGH E150 ASSIGNED

=> fil reg

FILE 'REGISTRY' ENTERED AT 19:06:05 ON 15 AUG 2002
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STRUCTURE FILE UPDATES: 14 AUG 2002 HIGHEST RN 443957-06-0
 DICTIONARY FILE UPDATES: 14 AUG 2002 HIGHEST RN 443957-06-0

TSCA INFORMATION NOW CURRENT THROUGH MAY 20, 2002

Please note that search-term pricing does apply when
 conducting SmartSELECT searches.

Crossover limits have been increased. See HELP CROSSOVER for details.

Calculated physical property data is now available. See HELP PROPERTIES
 for more information. See STNote 27, Searching Properties in the CAS
 Registry File, for complete details:
<http://www.cas.org/ONLINE/STN/STNOTES/stnotes27.pdf>

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=> d his 122

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L22 ANSWER 1 OF 125 REGISTRY COPYRIGHT 2002 ACS

RN 401914-69-0 REGISTRY

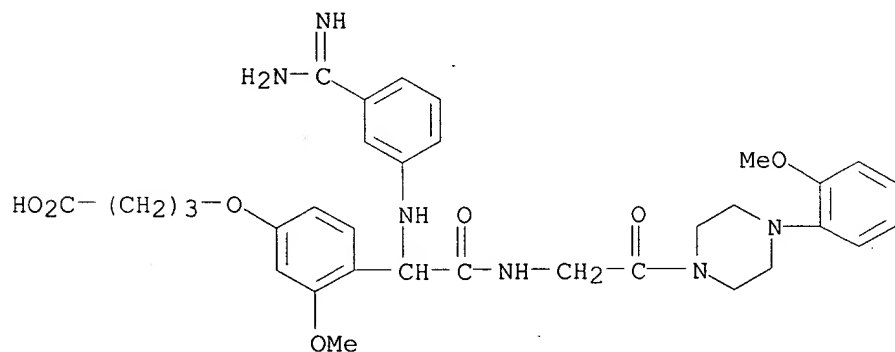
CN Butanoic acid, 4-[4-[1-[[3-(aminoiminomethyl)phenyl]amino]-2-[[2-[4-(2-methoxyphenyl)-1-piperazinyl]-2-oxoethyl]amino]-2-oxoethyl]-3-methoxyphenoxy]- (9CI) (CA INDEX NAME)

FS 3D CONCORD

MF C33 H40 N6 O7

SR CA

LC STN Files: CA, CAPLUS, TOXCENTER

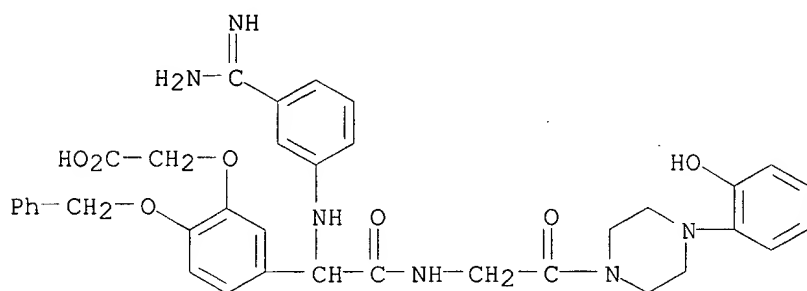


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1 REFERENCES IN FILE CAPLUS (1967 TO DATE)

REFERENCE 1: 136:216538

L22 ANSWER 5 OF 125 REGISTRY COPYRIGHT 2002 ACS
RN 401914-60-1 REGISTRY
CN Acetic acid, [5-[1-[[3-(aminoiminomethyl)phenyl]amino]-2-[[2-[4-(2-hydroxyphenyl)-1-piperazinyl]-2-oxoethyl]amino]-2-oxoethyl]-2-(phenylmethoxy)phenoxy]- (9CI) (CA INDEX NAME)
FS 3D CONCORD
MF C36 H38 N6 O7
SR CA
LC STN Files: CA, CAPLUS, TOXCENTER

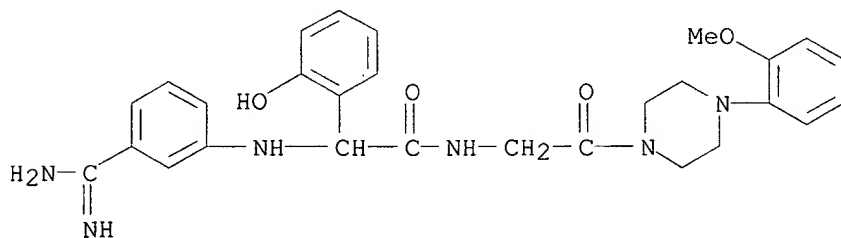


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1 REFERENCES IN FILE CAPLUS (1967 TO DATE)

REFERENCE 1: 136:216538

L22 ANSWER 10 OF 125 REGISTRY COPYRIGHT 2002 ACS
RN 401914-54-3 REGISTRY
CN Benzeneacetamide, .alpha.-[[3-(aminoiminomethyl)phenyl]amino]-2-hydroxy-N-[2-[4-(2-methoxyphenyl)-1-piperazinyl]-2-oxoethyl]- (9CI) (CA INDEX NAME)
FS 3D CONCORD
MF C28 H32 N6 O4
SR CA
LC STN Files: CA, CAPLUS, TOXCENTER



PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

1 REFERENCES IN FILE CA (1967 TO DATE)

1 REFERENCES IN FILE CAPLUS (1967 TO DATE)

REFERENCE 1: 136:216538

L22 ANSWER 15 OF 125 REGISTRY COPYRIGHT 2002 ACS

RN 401914-48-5 REGISTRY

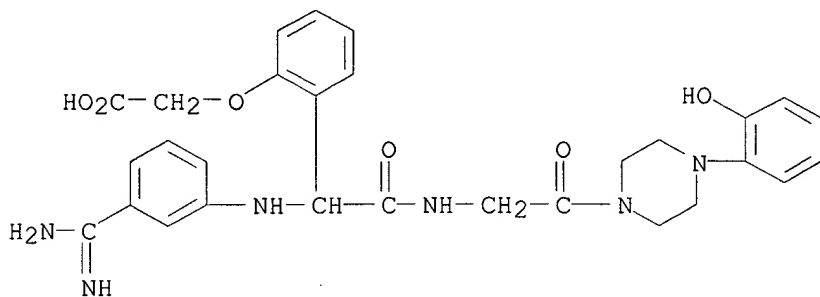
CN Acetic acid, [2-[1-[[3-(aminoiminomethyl)phenyl]amino]-2-[[2-[4-(2-hydroxyphenyl)-1-piperazinyl]-2-oxoethyl]amino]-2-oxoethyl]phenoxy]- (9CI)
(CA INDEX NAME)

FS 3D CONCORD

MF C29 H32 N6 O6

SR CA

LC STN Files: CA, CAPLUS, TOXCENTER



PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

1 REFERENCES IN FILE CA (1967 TO DATE)

1 REFERENCES IN FILE CAPLUS (1967 TO DATE)

REFERENCE 1: 136:216538

L22 ANSWER 20 OF 125 REGISTRY COPYRIGHT 2002 ACS

RN 401914-43-0 REGISTRY

CN Benzeneacetamide, .alpha.-[[3-(aminoiminomethyl)phenyl]amino]-2-(.beta.-D-glucopyranosyloxy)-N-[2-[4-(2-nitrophenyl)-1-piperazinyl]-2-oxoethyl]- (9CI) (CA INDEX NAME)

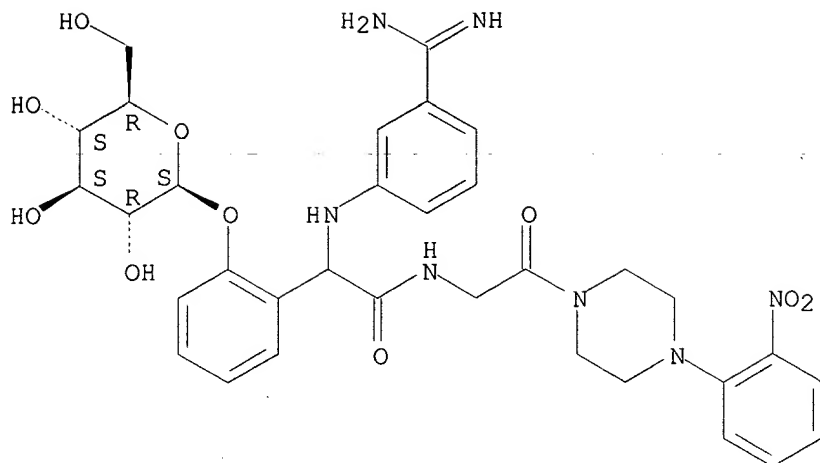
FS STEREOSEARCH

MF C33 H39 N7 O10

SR CA

LC STN Files: CA, CAPLUS, TOXCENTER

Absolute stereochemistry.

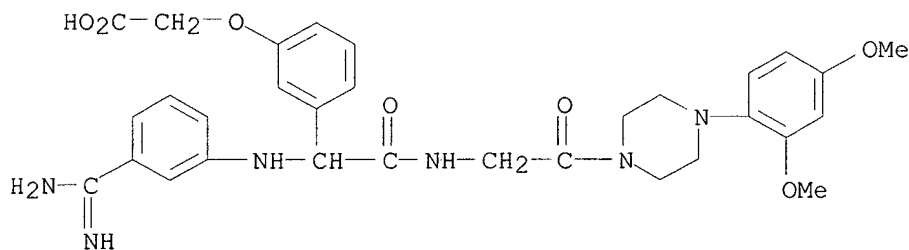


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1 REFERENCES IN FILE CAPLUS (1967 TO DATE)

REFERENCE 1: 136:216538

L22 ANSWER 25 OF 125 REGISTRY COPYRIGHT 2002 ACS
RN 401914-35-0 REGISTRY
CN Acetic acid, [3-[1-[[3-(aminoiminomethyl)phenyl]amino]-2-[[2-[4-(2,4-dimethoxyphenyl)-1-piperazinyl]-2-oxoethyl]amino]-2-oxoethyl]phenoxy]-(9CI) (CA INDEX NAME)
FS 3D CONCORD
MF C31 H36 N6 O7
SR CA
LC STN Files: CA, CAPLUS, TOXCENTER



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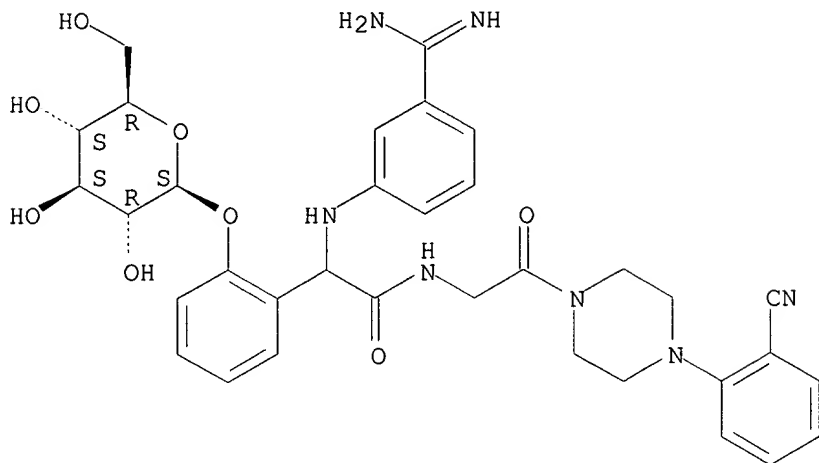
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1 REFERENCES IN FILE CAPLUS (1967 TO DATE)

REFERENCE 1: 136:216538

L22 ANSWER 30 OF 125 REGISTRY COPYRIGHT 2002 ACS
RN 401914-29-2 REGISTRY
CN Benzeneacetamide, .alpha.-[[3-(aminoiminomethyl)phenyl]amino]-N-[2-[4-(2-cyanophenyl)-1-piperazinyl]-2-oxoethyl]-2-(.beta.-D-glucopyranosyloxy)-(9CI) (CA INDEX NAME)

FS STEREOSEARCH
MF C34 H39 N7 O8
SR CA
LC STN Files: CA, CAPLUS, TOXCENTER

Absolute stereochemistry.



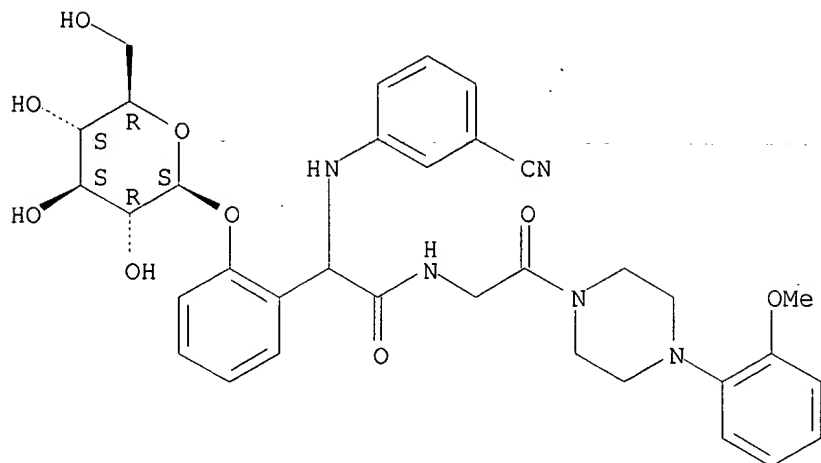
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1 REFERENCES IN FILE CA (1967 TO DATE)
1 REFERENCES IN FILE CAPLUS (1967 TO DATE)

REFERENCE 1: 136:216538

L22 ANSWER 35 OF 125 REGISTRY COPYRIGHT 2002 ACS
RN **401914-24-7** REGISTRY
CN Benzeneacetamide, .alpha.-[(3-cyanophenyl)amino]-2-(.beta.-D-glucopyranosyloxy)-N-[2-[4-(2-methoxyphenyl)-1-piperazinyl]-2-oxoethyl]-
(9CI) (CA INDEX NAME)
FS STEREOSEARCH
MF C34 H39 N5 O9
SR CA
LC STN Files: CA, CAPLUS, TOXCENTER

Absolute stereochemistry.

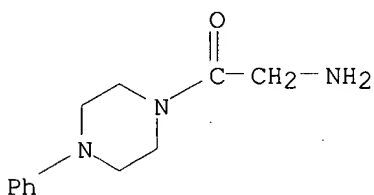


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1 REFERENCES IN FILE CAPLUS (1967 TO DATE)

REFERENCE 1: 136:216538

L22 ANSWER 43 OF 125 REGISTRY COPYRIGHT 2002 ACS
RN **359821-44-6** REGISTRY
CN Piperazine, 1-(aminoacetyl)-4-phenyl- (9CI) (CA INDEX NAME)
FS 3D CONCORD
MF C12 H17 N3 O
SR CA
LC STN Files: CA, CAPLUS, TOXCENTER

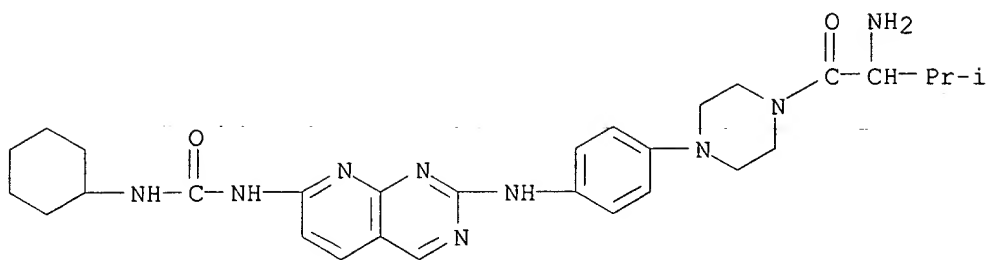


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1 REFERENCES IN FILE CAPLUS (1967 TO DATE)

REFERENCE 1: 135:226981

L22 ANSWER 44 OF 125 REGISTRY COPYRIGHT 2002 ACS
RN **352328-16-6** REGISTRY
CN Piperazine, 1-(2-amino-3-methyl-1-oxobutyl)-4-[4-[[7-
[[[(cyclohexylamino)carbonyl]amino]pyrido[2,3-d]pyrimidin-2-
yl]amino]phenyl]- (9CI) (CA INDEX NAME)
FS 3D CONCORD
MF C29 H39 N9 O2
SR CA
LC STN Files: CA, CAPLUS, TOXCENTER



PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

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1 REFERENCES IN FILE CAPLUS (1967 TO DATE)

REFERENCE 1: 135:152817

L22 ANSWER 46 OF 125 REGISTRY COPYRIGHT 2002 ACS

RN **343789-33-3** REGISTRY

CN Piperazine, 1-[(2R)-2-amino-1-oxopropyl]-4-[2-[5-(2-methoxyethoxy)-1H-benzimidazol-1-yl]-8-quinolinyl]- (9CI) (CA INDEX NAME)

OTHER NAMES:

CN (R)-2-Amino-1-[4-[2-[5-(2-methoxyethoxy)benzimidazol-1-yl]quinolin-8-yl]piperazin-1-yl]propan-1-one

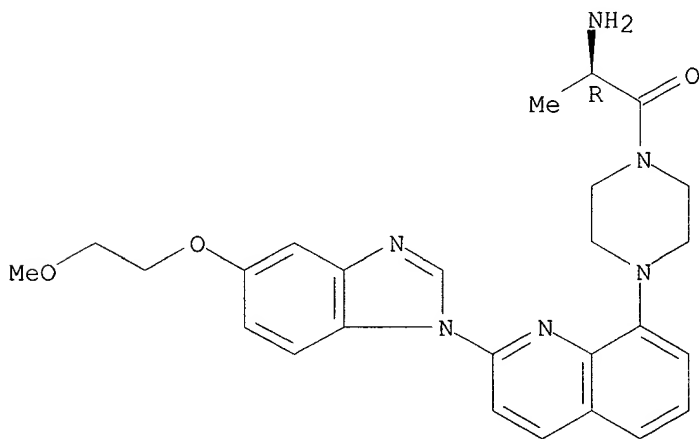
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LC STN Files: CA, CAPLUS, TOXCENTER

Absolute stereochemistry.



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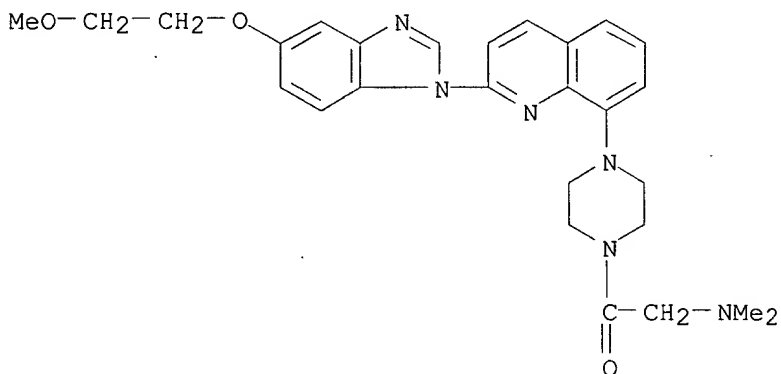
1 REFERENCES IN FILE CA (1967 TO DATE)
1 REFERENCES IN FILE CAPLUS (1967 TO DATE)

REFERENCE 1: 135:33479

L22 ANSWER 47 OF 125 REGISTRY COPYRIGHT 2002 ACS

RN **343788-96-5** REGISTRY

CN Piperazine, 1-[(dimethylamino)acetyl]-4-[2-[5-(2-methoxyethoxy)-1H-benzimidazol-1-yl]-8-quinolinyl]- (9CI) (CA INDEX NAME)
 OTHER NAMES:
 CN 2-Dimethylamino-1-[4-[2-[5-(2-methoxyethoxy)benzimidazol-1-yl]quinolin-8-yl]piperazin-1-yl]ethanone
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 MF C27 H32 N6 O3
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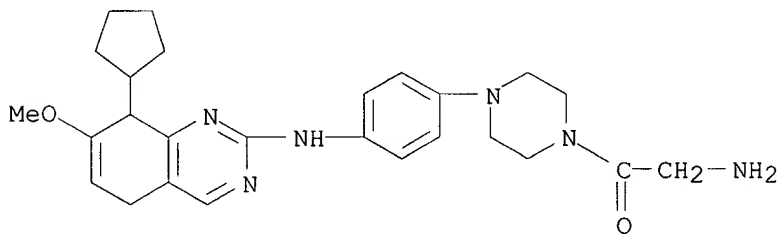


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 1 REFERENCES IN FILE CAPLUS (1967 TO DATE)

REFERENCE 1: 135:33479

L22 ANSWER 51 OF 125 REGISTRY COPYRIGHT 2002 ACS
 RN **342799-92-2** REGISTRY
 CN Piperazine, 1-(aminoacetyl)-4-[4-[(8-cyclopentyl-5,8-dihydro-7-methoxy-2-quinazolinyl)amino]phenyl]- (9CI) (CA INDEX NAME)
 FS 3D CONCORD
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 LC STN Files: CA, CAPLUS, TOXCENTER



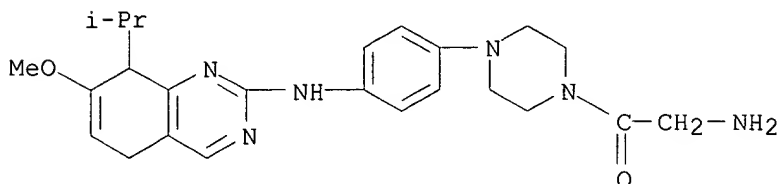
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REFERENCE 1: 135:19655

L22 ANSWER 55 OF 125 REGISTRY COPYRIGHT 2002 ACS

RN **342799-88-6** REGISTRY
 CN Piperazine, 1-(aminoacetyl)-4-[4-[[5,8-dihydro-7-methoxy-8-(1-methylethyl)-2-quinazolinyl]amino]phenyl]- (9CI) (CA INDEX NAME)
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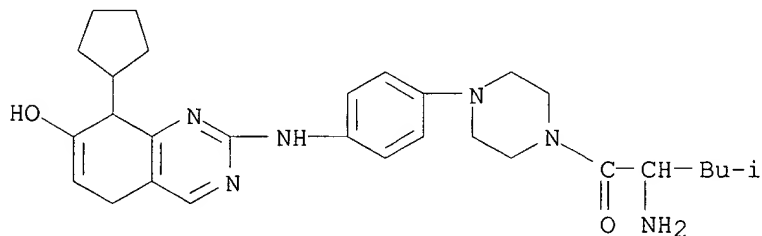


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 1 REFERENCES IN FILE CAPLUS (1967 TO DATE)

REFERENCE 1: 135:19655

L22 ANSWER 60 OF 125 REGISTRY COPYRIGHT 2002 ACS
 RN **342799-83-1** REGISTRY
 CN Piperazine, 1-(2-amino-4-methyl-1-oxopentyl)-4-[4-[(8-cyclopentyl-5,8-dihydro-7-hydroxy-2-quinazolinyl)amino]phenyl]- (9CI) (CA INDEX NAME)
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 LC STN Files: CA, CAPLUS, TOXCENTER

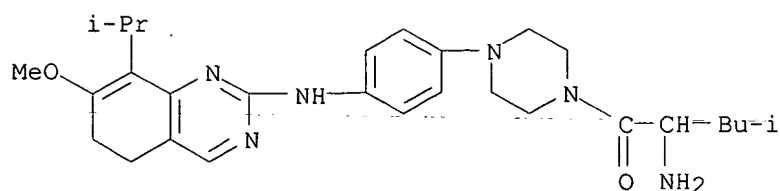


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REFERENCE 1: 135:19655

L22 ANSWER 65 OF 125 REGISTRY COPYRIGHT 2002 ACS
 RN **342799-78-4** REGISTRY
 CN Piperazine, 1-(2-amino-4-methyl-1-oxopentyl)-4-[4-[[5,6-dihydro-7-methoxy-8-(1-methylethyl)-2-quinazolinyl]amino]phenyl]- (9CI) (CA INDEX NAME)
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 LC STN Files: CA, CAPLUS, TOXCENTER

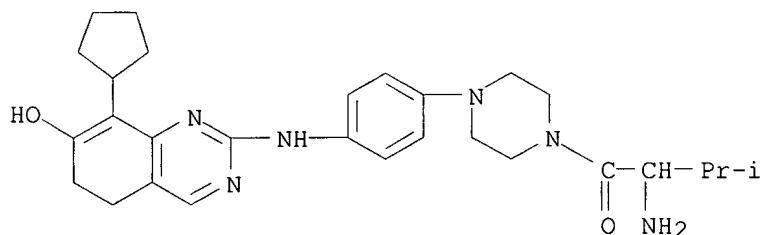


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REFERENCE 1: 135:19655

L22 ANSWER 70 OF 125 REGISTRY COPYRIGHT 2002 ACS
RN **342799-73-9** REGISTRY
CN Piperazine, 1-(2-amino-3-methyl-1-oxobutyl)-4-[4-[(8-cyclopentyl-5,6-dihydro-7-hydroxy-2-quinazolinyl)amino]phenyl]- (9CI) (CA INDEX NAME)
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LC STN Files: CA, CAPLUS, TOXCENTER

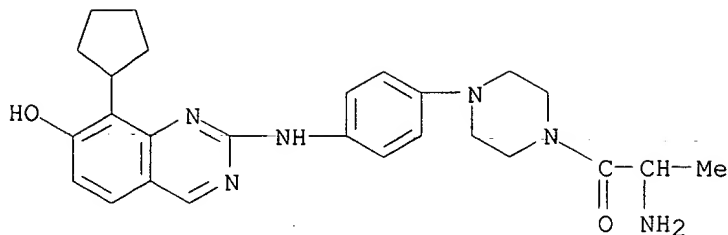


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REFERENCE 1: 135:19655

L22 ANSWER 75 OF 125 REGISTRY COPYRIGHT 2002 ACS
RN **342798-92-9** REGISTRY
CN Piperazine, 1-(2-amino-1-oxopropyl)-4-[4-[(8-cyclopentyl-7-hydroxy-2-quinazolinyl)amino]phenyl]- (9CI) (CA INDEX NAME)
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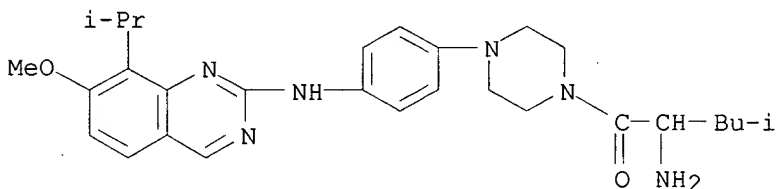


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REFERENCE 1: 135:19655

L22 ANSWER 80 OF 125 REGISTRY COPYRIGHT 2002 ACS
RN **342798-55-4** REGISTRY
CN Piperazine, 1-(2-amino-4-methyl-1-oxopentyl)-4-[4-[[7-methoxy-8-(1-methylethyl)-2-quinazolinyl]amino]phenyl]- (9CI) (CA INDEX NAME)
FS 3D CONCORD
MF C28 H38 N6 O2
SR CA
LC STN Files: CA, CAPLUS, TOXCENTER



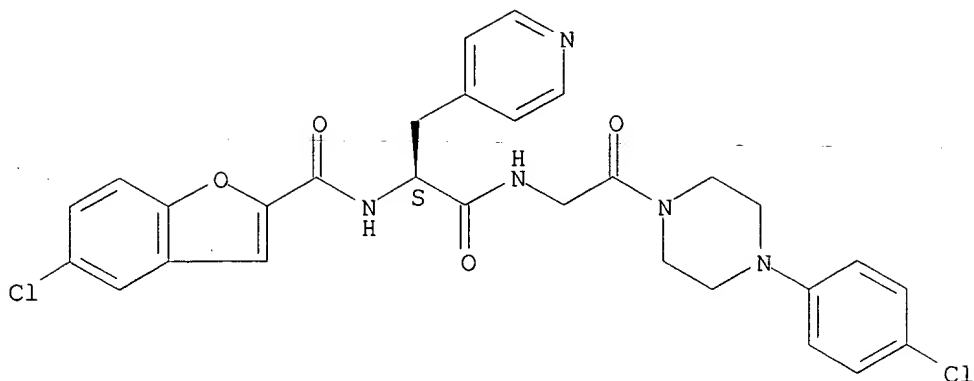
PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

1 REFERENCES IN FILE CA (1967 TO DATE)
1 REFERENCES IN FILE CAPLUS (1967 TO DATE)

REFERENCE 1: 135:19655

L22 ANSWER 87 OF 125 REGISTRY COPYRIGHT 2002 ACS
RN **337530-82-2** REGISTRY
CN 4-Pyridinepropanamide, .alpha.-[[[(5-chloro-2-benzofuranyl)carbonyl]amino]-N-[2-[4-(4-chlorophenyl)-1-piperazinyl]-2-oxoethyl]-, (.alpha.S)- (9CI) (CA INDEX NAME)
FS STEREOSEARCH
MF C29 H27 Cl2 N5 O4
SR CA
LC STN Files: CA, CAPLUS, TOXCENTER

Absolute stereochemistry.



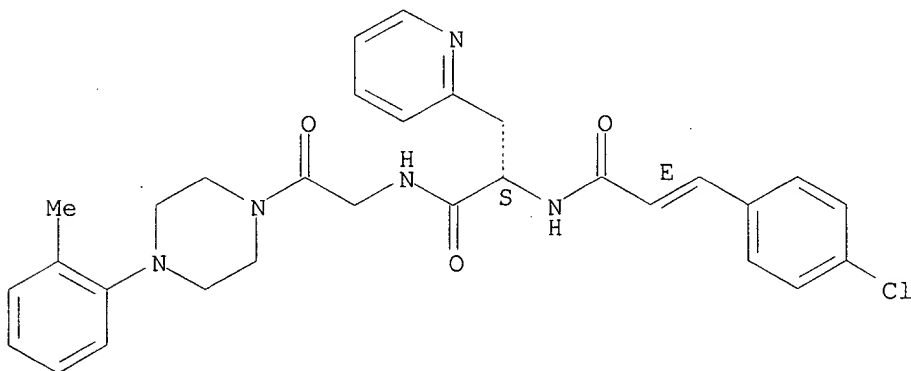
PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

1 REFERENCES IN FILE CA (1967 TO DATE)
1 REFERENCES IN FILE CAPLUS (1967 TO DATE)

REFERENCE 1: 134:340709

L22, ANSWER 90 OF 125 REGISTRY COPYRIGHT 2002 ACS
RN **337530-79-7** REGISTRY
CN 2-Pyridinepropanamide, .alpha.-[[(2E)-3-(4-chlorophenyl)-1-oxo-2-propenyl]amino]-N-[2-[4-(2-methylphenyl)-1-piperazinyl]-2-oxoethyl]-, (.alpha.S)- (9CI) (CA INDEX NAME)
FS STEREOSEARCH
MF C30 H32 Cl N5 O3
SR CA
LC STN Files: CA, CAPLUS, TOXCENTER

Absolute stereochemistry.
Double bond geometry as shown.



PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

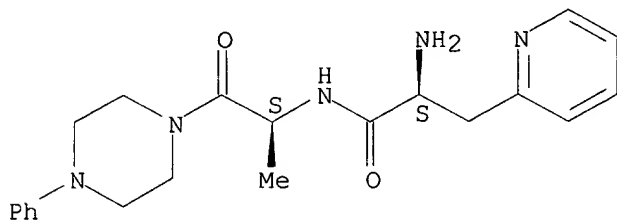
1 REFERENCES IN FILE CA (1967 TO DATE)
1 REFERENCES IN FILE CAPLUS (1967 TO DATE)

REFERENCE 1: 134:340709

L22 ANSWER 95 OF 125 REGISTRY COPYRIGHT 2002 ACS
RN **337530-74-2** REGISTRY

CN 2-Pyridinepropanamide, .alpha.-amino-N-[(1S)-1-methyl-2-oxo-2-(4-phenyl-1-piperazinyl)ethyl]-, trihydrochloride, (.alpha.S)- (9CI) (CA INDEX NAME)
 FS STEREOSEARCH
 MF C21 H27 N5 O2 . 3 Cl H
 SR CA
 LC STN Files: CA, CAPLUS, TOXCENTER

Absolute stereochemistry.



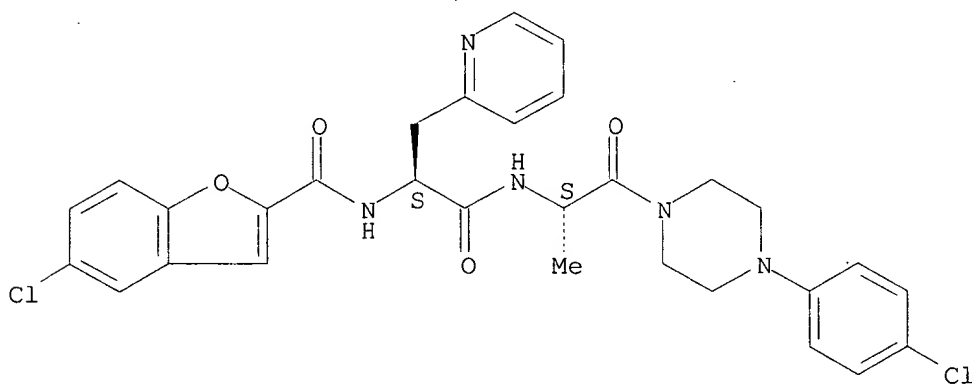
● 3 HCl

1 REFERENCES IN FILE CA (1967 TO DATE)
 1 REFERENCES IN FILE CAPLUS (1967 TO DATE)

REFERENCE 1: 134:340709

L22 ANSWER 100 OF 125 REGISTRY COPYRIGHT 2002 ACS
 RN 337530-69-5 REGISTRY
 CN 2-Pyridinepropanamide, .alpha.-[[[(5-chloro-2-benzofuranyl)carbonyl]amino]-N-[(1S)-2-[4-(4-chlorophenyl)-1-piperazinyl]-1-methyl-2-oxoethyl]-, (.alpha.S)- (9CI) (CA INDEX NAME)
 FS STEREOSEARCH
 MF C30 H29 Cl2 N5 O4
 SR CA
 LC STN Files: CA, CAPLUS, TOXCENTER

Absolute stereochemistry.



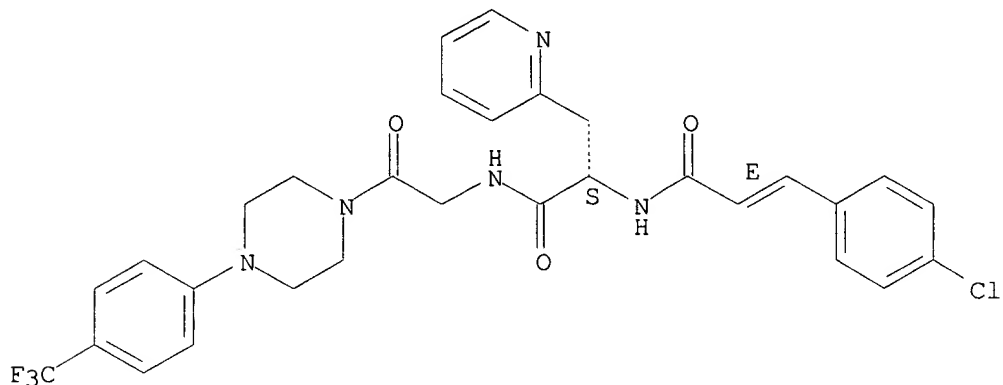
PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

1 REFERENCES IN FILE CA (1967 TO DATE)
 1 REFERENCES IN FILE CAPLUS (1967 TO DATE)

REFERENCE 1: 134:340709

L22 ANSWER 105 OF 125 REGISTRY COPYRIGHT 2002 ACS
 RN **337530-64-0** REGISTRY
 CN 2-Pyridinepropanamide, .alpha.-[[(2E)-3-(4-chlorophenyl)-1-oxo-2-propenyl]amino]-N-[2-oxo-2-[4-[4-(trifluoromethyl)phenyl]-1-piperazinyl]ethyl]-, (.alpha.S)- (9CI) (CA INDEX NAME)
 FS STEREOSEARCH
 MF C30 H29 Cl F3 N5 O3
 SR CA
 LC STN Files: CA, CAPLUS, TOXCENTER

Absolute stereochemistry.
 Double bond geometry as shown.



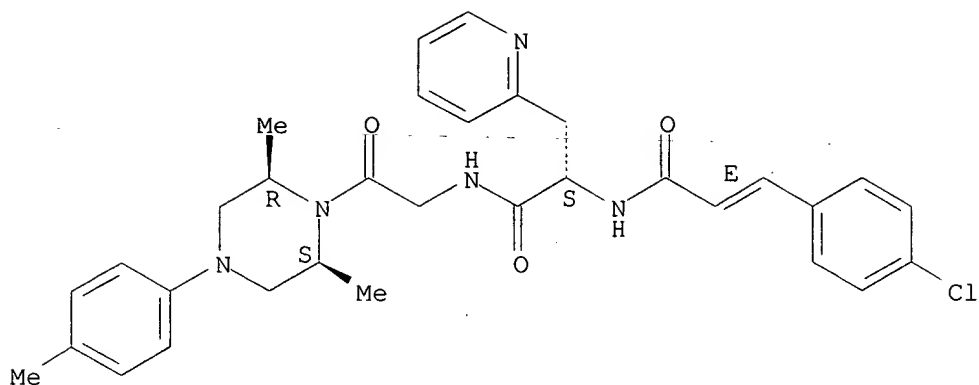
PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

1 REFERENCES IN FILE CA (1967 TO DATE)
 1 REFERENCES IN FILE CAPLUS (1967 TO DATE)

REFERENCE 1: 134:340709

L22 ANSWER 110 OF 125 REGISTRY COPYRIGHT 2002 ACS
 RN **337530-40-2** REGISTRY
 CN 2-Pyridinepropanamide, .alpha.-[[(2E)-3-(4-chlorophenyl)-1-oxo-2-propenyl]amino]-N-[2-[(2R,6S)-2,6-dimethyl-4-(4-methylphenyl)-1-piperazinyl]-2-oxoethyl]-, (.alpha.S)- (9CI) (CA INDEX NAME)
 FS STEREOSEARCH
 MF C32 H36 Cl N5 O3
 SR CA
 LC STN Files: CA, CAPLUS, TOXCENTER

Absolute stereochemistry.
 Double bond geometry as shown.



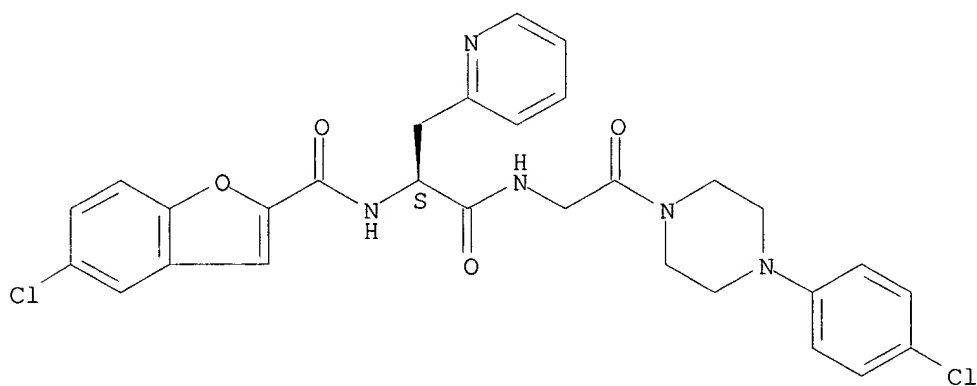
PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

1 REFERENCES IN FILE CA (1967 TO DATE)
1 REFERENCES IN FILE CAPLUS (1967 TO DATE)

REFERENCE 1: 134:340709

L22 ANSWER 115 OF 125 REGISTRY COPYRIGHT 2002 ACS
RN **337530-26-4** REGISTRY
CN 2-Pyridinepropanamide, .alpha.-[[(5-chloro-2-benzofuranyl)carbonyl]amino]-
N-[2-[4-(4-chlorophenyl)-1-piperazinyl]-2-oxoethyl]-, (.alpha.S)- (9CI)
(CA INDEX NAME)
FS STEREOSEARCH
MF C29 H27 Cl2 N5 O4
SR CA
LC STN Files: CA, CAPLUS, TOXCENTER

Absolute stereochemistry.



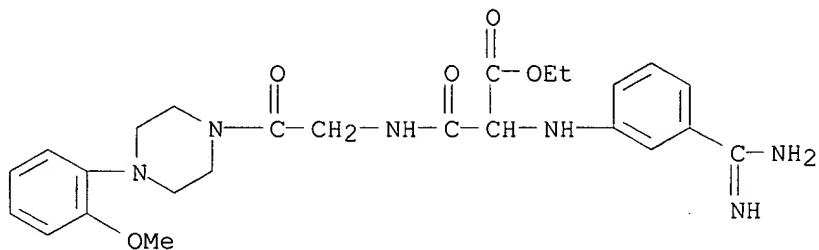
PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

1 REFERENCES IN FILE CA (1967 TO DATE)
1 REFERENCES IN FILE CAPLUS (1967 TO DATE)

REFERENCE 1: 134:340709

L22 ANSWER 120 OF 125 REGISTRY COPYRIGHT 2002 ACS
RN **328552-43-8** REGISTRY

CN Alanine, N-[3-(aminoiminomethyl)phenyl]-3-[[2-[4-(2-methoxyphenyl)-1-piperazinyl]-2-oxoethyl]amino]-3-oxo-, ethyl ester, hydrochloride (9CI)
(CA INDEX NAME)
MF C25 H32 N6 O5 . x Cl H
SR CA
LC STN Files: CA, CAPLUS, TOXCENTER

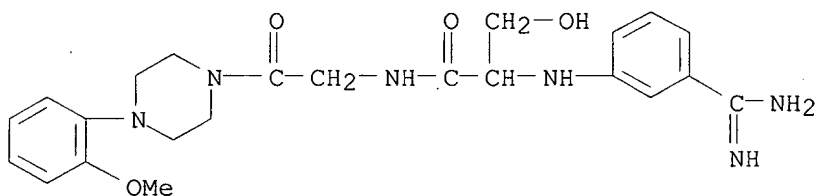


●x HCl

1 REFERENCES IN FILE CA (1967 TO DATE)
1 REFERENCES IN FILE CAPLUS (1967 TO DATE)

REFERENCE 1: 134:208135

L22 ANSWER 121 OF 125 REGISTRY COPYRIGHT 2002 ACS
RN **328551-48-0** REGISTRY
CN Propanamide, 2-[[3-(aminoiminomethyl)phenyl]amino]-3-hydroxy-N-[2-[4-(2-methoxyphenyl)-1-piperazinyl]-2-oxoethyl]-, hydrochloride (9CI) (CA INDEX NAME)
MF C23 H30 N6 O4 . x Cl H
SR CA
LC STN Files: CA, CAPLUS, TOXCENTER

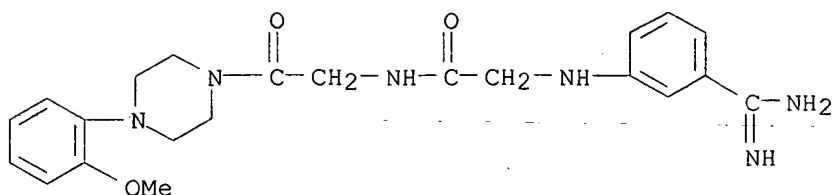


●x HCl

1 REFERENCES IN FILE CA (1967 TO DATE)
1 REFERENCES IN FILE CAPLUS (1967 TO DATE)

REFERENCE 1: 134:208135

L22 ANSWER 123 OF 125 REGISTRY COPYRIGHT 2002 ACS
RN **328550-92-1** REGISTRY
CN Acetamide, 2-[[3-(aminoiminomethyl)phenyl]amino]-N-[2-[4-(2-methoxyphenyl)-1-piperazinyl]-2-oxoethyl]-, hydrochloride (9CI) (CA INDEX NAME)
MF C22 H28 N6 O3 . x Cl H
SR CA
LC STN Files: CA, CAPLUS, TOXCENTER



● x HCl

1 REFERENCES IN FILE CA (1967 TO DATE)
1 REFERENCES IN FILE CAPLUS (1967 TO DATE)

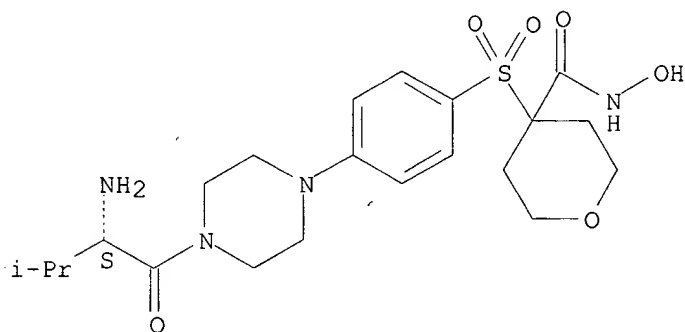
REFERENCE 1: 134:208135

L22 ANSWER 124 OF 125 REGISTRY COPYRIGHT 2002 ACS
RN **226393-14-2** REGISTRY
CN 2H-Pyran-4-carboxamide, 4-[[4-[4-[(2S)-2-amino-3-methyl-1-oxobutyl]-1-piperazinyl]phenyl]sulfonyl]tetrahydro-N-hydroxy-, bis(trifluoroacetate) (salt) (9CI) (CA INDEX NAME)
FS STEREOSEARCH
MF C21 H32 N4 O6 S . 2 C2 H F3 O2
SR CA
LC STN Files: CA, CAPLUS, TOXCENTER, USPATFULL

CM 1

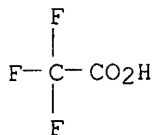
CRN 226393-13-1
CMF C21 H32 N4 O6 S

Absolute stereochemistry.



CM 2

CRN 76-05-1
CMF C2 H F3 O2



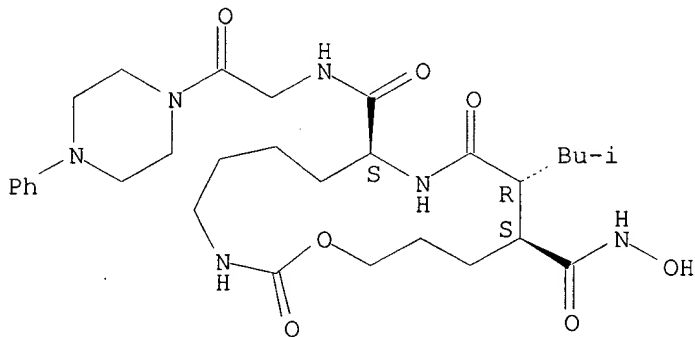
2 REFERENCES IN FILE CA (1967 TO DATE)
2 REFERENCES IN FILE CAPLUS (1967 TO DATE)

REFERENCE 1: 133:193079

REFERENCE 2: 131:18929

L22 ANSWER 125 OF 125 REGISTRY COPYRIGHT 2002 ACS
RN 215938-51-5 REGISTRY
CN 1-Oxa-3,9-diazacyclopentadecane-8,12-dicarboxamide, N12-hydroxy-11-(2-methylpropyl)-2,10-dioxo-N8-[2-oxo-2-(4-phenyl-1-piperazinyl)ethyl]-, (8S,11R,12S)- (9CI) (CA INDEX NAME)
FS STEREOSEARCH
MF C30 H46 N6 O7
SR CA
LC STN Files: CA, CAPLUS, TOXCENTER

Absolute stereochemistry.



PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

2 REFERENCES IN FILE CA (1967 TO DATE)
2 REFERENCES IN FILE CAPLUS (1967 TO DATE)

REFERENCE 1: 135:226981

REFERENCE 2: 130:14260